

6 November 1980

What are the research councils for?

This week will be a testing time for the research councils which are one of the principal means of support for British scientific research. Both the Medical and Science Research Councils are due to publish their annual reports. Hard on the heels of the annual report of the Natural Environment Research Council (see *Nature* 28 October) these documents will between them provide an opportunity for telling where the research councils collectively are heading. Naturally, readers of these annual reports will have to be prepared to read between the lines. Such reports begin with a more or less ritual recitation of honours bestowed on members of the staff and of visits by members of the royal family to council establishments. These days, there usually follows an account of the difficulties of living within a budget which, if not actually shrinking in real terms, is no longer growing. Occasionally, a council may be so moved by some particular consequence of straitened budgets that it will specifically draw attention to the collapse of some special project. This was the spirit in which the Natural Environment Research Council last week let it be known that the Geological Survey of Britain is now jeopardized by the unwillingness of the Department of the Environment to contribute to its continuing cost. Usually, however, the councils tell their tale with as little commotion as they can.

This year things could — or should — be different. No amount of built-in gentility can conceal from the councils themselves the increasing difficulty of sharing out the funds that come their way from the Department of Education and Science in ways that are likely to be both equitable (as between deserving claimants) and effective (in promoting research of high quality and promise). The collapse of the dual-support system is another problem. If the University Grants Committee can no longer ensure that university departments are well-equipped to conduct research, the research councils must either break with their present practice of not financing basic facilities (which means making fewer grants) or must acknowledge that much of what they spend will be used with less than full effectiveness. The trouble is that there is very little that research councils acting individually can do to shape a more rational pattern for academic research. So long as they stick (as they should) to the principle that grants go to the best applicants, they are bound to find themselves spreading their resources more thinly than is reasonable. This recognition is no doubt part of the reason why the Advisory Board for the Research Councils has set up (with the Committee of Vice-Chancellors and Principals, representing the university sector) the Merrison Committee. The hope is that the committee will be able to evolve a framework within which the old goals of concentrating academic research on selected universities (or university departments) can be made acceptable. It remains to be seen whether the University Grants Committee has the stomach for implementing whatever policy may emerge — and whether the universities will allow it to do so.

The research councils will also be perplexed this year by signs of the possible collapse of the Rothschild system with which they have been living since 1971. So they should be. One among them, the Medical Research Council, has been able to claw back from the Department of Health the now inflated funds taken away progressively in the years after 1973 (see *Nature* 23 October). Others will be tempted to follow suit, and will earn a dusty answer from the government departments concerned. Sir Hermann Bondi, the new chairman of the Natural Environment Research Council, says that he supports the notion that government departments should act as customers for research (see page 5). Will he be of the same opinion when he discovers how vulnerable

his new council is to inconstancy or even downright fickleness on the part of sponsoring ministries?

The trouble with customers is that they are often wrong, but that their actions inevitably create the illusion that they are right. The decision by the Department of the Environment to cut back its contributions to the British Geological Survey can have one of two consequences. Either the survey will be supported by other means (in which case the department will congratulate itself on having saved some money) or it will be stopped; the United Kingdom will not on that account collapse and the department will take pride in having helped bring an apparently worthless activity to an end. Either way, the customer will seem right. Nobody will have made a serious examination of the value of the Geological Survey.

Taken together, these developments are likely to provoke further soul-searching among the research councils and their sponsors. For the Medical Research Council, the most immediate question is whether it can turn from its largely academic ways so as to earn the £12 million a year it will now have to spend on applied medical research. For all of them, the long-term question is how their functions are to be defined and carried out. During the past Rothschild decade, their relative budgets have hardly changed. Each year, one or two of the councils have had an extra one or two per cent in real terms to spend, while the others have fallen back. But is there any reason to suppose that the sums being spent on research in agriculture, medicine and the natural environment in 1970 are still appropriate a decade later? And is it right that the budget of the Science Research Council, exempted from the rigours of Rothschild, should stand in exactly the same relationship with those of what would be called, in the United States, the "mission-oriented" councils? Can it serve either the interests of research or of the public purse that these increasingly elaborate organizations should just grow, like Topsy?

This is why there is emerging an urgent need for yet another review of what the research councils are for. Although it would be convenient that the review should wait until the Merrison inquiry is completed, that is largely a recipe for postponing until tomorrow what should be undertaken right away. The agenda for an inquiry is, after all, easily conceived. Indeed, the final report of such an inquiry should not unduly tax the imagination.

The research councils have two quite different functions, which collectively they must keep. Two of them were set up to sponsor basic research relevant to the practice of agriculture and medicine. A third, the Natural Environment Research Council, is historically an exercise in wish-fulfilment — it was set up in the early 1960s in the hope that it could put flesh on the bones of the then nascent belief that problems of the environment and natural resources would dominate the remainder of the century. The belief has been justified, but the council has turned out to be a manager of a miscellaneous collection of disparate enterprises. (Presumably part of the reason for putting the organization in the hands of Sir Hermann Bondi is that he may be able to weld them into a more coherent whole; but he will have his work cut out.) Almost incidentally, these three research councils help to foster academic research, partly through research grants to academics, partly by links between their research institutes and neighbouring universities. Both kinds of links are valuable, and should be preserved at all costs.

Change is needed elsewhere, and in particular in the definition of the practical functions of the councils with a mission. In medicine, can it make sense that the Medical Research Council



should take back responsibility for the Rothschild money but still stand only on the sidelines in the support of teaching hospitals and the administration of research within the National Health Service? In agriculture, there is also a case for asking that the old boundary between "basic" and "applied" research should be made more flexible. British agriculture has been uncommonly successful in the past few decades. It might have been even more

successful if the customers and the contractors had lived more in each others' pockets. In short, if the Rothschild recipe is now to be eroded, there are the strongest reasons why the balance should be tilted the other way and the research councils given even more practical marching orders than in the recent past. If, at the same time, they can keep their links with the universities, everybody will be the beneficiary.

Ideological trouble ahead for Unesco

The United Nations Educational, Scientific and Cultural Organization (Unesco) seems bent on cutting its own throat. The General Assembly of the organization just ended in Belgrade has confirmed that Unesco is no longer the high-minded arm of the United Nations concerned with the general enlightenment that recruited the late Sir Julian Huxley as its first director-general. To be sure, last month's proceedings were less sordidly political than those in the past decade when general assemblies were used by the member states as occasions for isolating Israel from Unesco's general activities. The Belgrade assembly was, rather, cynically political. On two important matters, a combination of developing countries (the "group of seventy-seven") and the Eastern bloc was able to force down the throats of the chief contributors to the Unesco budget two thoroughly bad proposals — a controversial resolution about the procedures to be used for the gathering of news throughout the world, and a scheme for the setting up of a "Special Programme" for planning the technical development of developing countries, a kind of hangover from last year's United Nations Conference on Science and Technology at Vienna. Unesco's budget is to be increased by seven per cent (in real terms) to pay for these new ventures. The industrialized Western states who are the chief contributors have to pay up or get out.

The argument about news-gathering is not merely a technical matter of how news agencies operating internationally should be regulated, but an issue of principle going to the root of Unesco's existence. For several years, developing countries have been grumbling about the unpalatable news of their affairs frequently reported by journalists and news agencies from overseas. Unesco responded by mounting a study of the problem by a commission under Mr Sean McBride, a retired Irish diplomat. The McBride report has been a focus of controversy for the past two years, principally because it gave developing countries reason to believe that they are indeed exploited, and even dealt with unfairly, by the international news agencies. So, the argument goes, there must be a "new information order" to match the "new economic order" for which developing countries (with some justice) have been asking for several years. At Belgrade last month, Unesco was given until 1983 to work out the principles on which such a regime should be based.

But why should this be a black mark for Unesco? Surely the gathering of information is properly within the organization's terms of reference? And surely it is right and proper that it should respond to the wishes of the majority of its members? That is the defence of what Unesco is about. These arguments are nevertheless too facile. They entirely overlook the dangers of admitting that governments have a right to expect news of a kind that is welcome, even flattering. The enterprise on which Unesco is embarked also carries explicit approval for the notion that governments should properly be concerned with the management of the means by which news of their own doings is relayed to the wider world. The fear is that governments will use the Unesco resolution as an excuse for telling journalists what they should say.

It is, of course, well known that member governments differ in their estimation of these dangers. Many socialist states take the view, logical enough, that the gathering of information and its dissemination plays such an important role in society that governments must shoulder the responsibility. Most Western governments, with more or less enthusiasm, follow the opposite principle that a free press is a necessary guarantee of personal

freedom and thus of a just society. The governments of developing countries differ among themselves. Some hanker after the Eastern way but lack the facilities. Others — India is perhaps the most creditable example — put up with a free press without too much complaint. Wherever the truth lies (and there is not much doubt of that), the difference is frankly ideological. By backing one side and not the other, Unesco's members have unwisely — some would say foolishly — committed the organization to an ideological position in a way that must surely conflict with its high-minded principles.

Unesco's special programme for redressing the technical balance between the developing and the industrialized countries of the world is similarly born of ideology. Again, there is no complaint that the topic is outside the organization's terms of reference. Nor is it denied that there is an urgent need of more and of more effective technical and financial assistance for the developing countries of the world. There is yet a chance that the message of the Brandt Commission's study will sink in (see *Nature* 21 February). It does not, however, follow that the nostrums that preoccupied the Vienna conference last year would have been effective even if they had been approved (which they were not), that the notion of a "new technological order", ill-defined as it is, makes any sense and that a specially created Unesco secretariat, politicized as it would be, would be competent to define a strategy for the future. It is not, in any case, as if the United Nations system is short of organizations for fostering technical and economic development. Within its special terms of reference, Unesco might have done a useful job by helping to bring about a better understanding of the sharp differences of opinion that abound on the proper relationship between developed and developing countries on science and technology. By plumping for the solution of the new technological order, the majority of Unesco's members have jet again put ideology before good sense.

Unesco is not well placed to take such risks. Over the years, it has won itself an unenviable reputation for unreality, extravagance and maladministration. Some good things have come out of the splendid Corbusier building in the Place de Fontenay. Unesco helped to focus interest on Abu Simbel and on the hydrology of Venice. Its efforts to encourage innovation in science teaching and the systematization of scientific bibliographies have been well meaning but not sufficiently energetic to make a mark in competition with other free-wheeling agencies. Other projects, the so-called "Biosphere" programme for example, have been chiefly valuable as sources of largely empty generalizations. It is no wonder that people (and member governments) increasingly ask whether it can be worth its cost.

Unesco would be better placed to run ideological risks if it were less open to complaint about the ordinary conduct of its affairs. The chances are that most of the disaffected Western governments will react to the troubles at Belgrade by resolving to pay more attention to Unesco's business in the years immediately ahead. Few of them would wish, at this stage, to incur the opprobrium of taking the initiative to cut it down to size or even to put it to sleep. But things could change — as the United States Congress will change in January. Unesco may yet find itself in the uncomfortable position of the International Labour Organization, which has not yet recovered from the withdrawal of the United States three years ago. It would be unfortunate, but no by any means the end of the world, if Unesco were to find itself in a similar position. The remedy is in its own hands.

Academics agonize about weapons labs

Livermore and Los Alamos up for grabs

San Francisco

In what promises to be another stormy round in a long-running debate, the Board of Regents of the University of California is meeting next week to discuss how it should increase its control of research programmes at the two weapons laboratories which the university runs for the Department of Energy (DoE).

The present five-year management contract for the two laboratories — at Livermore and Los Alamos — runs out in 1982, and preliminary moves to negotiate a new contract with the department have restimulated discussion of the implications of the university's responsibility for the research that underpins a major part of the world's nuclear arsenal.

Last year, the Board of Regents, which is responsible to the state for the university's affairs, rejected a proposal from *ex-officio* member Governor Jerry Brown to remove all military research from the Lawrence Livermore Laboratory, and in September voted to open discussions with DoE for a new contract. The focus of debate has therefore shifted from whether the Livermore Laboratory should be carrying out weapons research at all to how the university should exercise its management responsibilities over this research. In particular, opinions differ about the extent to which the Board of Regents — and possibly outside advisers — should be involved in determining research priorities for the laboratory.

Under the present arrangement the university accepts responsibility for the quality of the research but leaves priorities almost entirely to DoE, a situation which many scientists and administrators at the laboratory are reluctant to see changed. "If a car is running well, you don't tamper with the engine", one Livermore official said last week.

Some members of the university faculty are, however, concerned about the lack of control over military research programmes. The autonomy enjoyed by the laboratories under the protection of the university was described in a report as "so delightful as to border on the licentious". More recently, a group of laboratory staff at Livermore, known as the Society of Professional Scientists and Engineers, has suggested that there should be greater outside monitoring of research.

At the same time, the university is keen to keep a contract which brings in \$4 million a year in management fees, and it

points out that several recent reports, including one prepared by the department's Energy Research Advisory Board, have concluded that it is in the best interests of both sides that the basic links with the university be maintained.

At its meeting last month, the Board of Regents received two proposals for modifying the relationship. Professor William Fretter, the university's vice-president, suggested that the regents appoint a new oversight committee to "provide increased accountability to the general public", and that this committee establish three evaluation committees, one of which would be responsible for establishing research priorities.

The second proposal came from Governor Brown and is based on the report of a committee which the university itself set up in 1978. Like Professor Fretter, the governor also proposes a new oversight committee, but this time assisted by an independent advisory board.

The two proposals agree on many points, but also have significant differences. For example, while the evaluation committees proposed by Professor Fretter would essentially be subcommittees of the oversight committee, Governor Brown's advisory committee would have much greater autonomy, being empowered to request that the oversight committee help it evaluate particular programmes or problems.

The composition of the proposed committees would also differ significantly. The evaluation committees proposed by Professor Fretter would chiefly consist of experts from within and outside the university. In contrast, Governor Brown

contemplates an advisory board of scientists, faculty members, students, health experts, theologians and others.

The president's office is now deciding whether the two proposals can be combined. Otherwise, the choice between the two approaches will have to be made by the regents.

Whatever the result, increased control — at least of research not related to weapons, which forms about half of the work of both laboratories — seems inevitable. The university's president, Dr David Saxon, has already proposed setting up a panel of scientists to recommend research priorities in energy research and other unclassified areas at the two laboratories.

More controversial is the extent to which an oversight committee should be involved in policy decisions about weapons research, which is shortly expected to include work on the MX missile system. Here both university and laboratory officials argue that all such policy decisions must be made at the national level in Washington, and that the laboratories should only carry out Washington's requests.

Critics point out, however, that in the past laboratory officials have been far from neutral in policy debates over weapons research and related areas of arms control. For example, pressures from the two weapons laboratories were significant in reducing the scope of the Comprehensive Test-Ban Treaty now being negotiated in Geneva, while other laboratory officials have been active in the debate over whether to ratify the Strategic Arms Limitation Treaty (Salt II).

David Dickson

Short commons for Spanish research

A ten-month freeze on research grants for scientists in Spanish universities and the Spanish National Research Council ended on 20 October with the distribution of 3,600 million pesetas (£22 million) to groups in the universities and the research council. The average of £24,000 per group must officially last three years — although the period may in practice be longer. Grants were last awarded in 1976.

The distribution has come in for some severe criticism, particularly from members of the group of 200 leading scientists who, just before the grants were announced, had sent a manifesto to the Minister of Universities and Research describing his policies as "derelict" (*Nature* 23 October, p.674). The group now says that the meagre distribution is no surprise. Spain historically has spent only 0.3 per cent of its gross national product (GNP) on research and development compared with about 2 per cent in other Western countries. Passions have,

however, been stirred by the way in which this distribution has been made.

One member of the group says that a key advisory body has been ignored, and that grants have been awarded by subject panels which were not best qualified to make judgements. The result has been a largely random distribution of money, he claims. Some of these discontents were aired at the meeting on European Economic Community (EEC) science policy held two weeks ago in Strasbourg.

The advisory body, the Gabinete de Estudios, was set up four years ago by the now deputy director-general of the United Nations Educational, Scientific and Cultural Organization, Professor Federico Mayor, to provide baseline studies of science in Spain and to advise the Comisión Asesora de Investigación Científica y Técnica (CACT), which distributed last month's grants. But the Gabinete's recommendations of referees for the grant applications were rejected, said the

manifesto spokesman, and CACT took other advice about the composition of the panels of referees.

One curious feature of the grant-making process is that the director of CACT, Professor Marcos Rico, demanded that nobody who was applying for a grant should serve on a review panel. The manifesto group complains that no scientist worth his salt would not be applying after a year without a research grant. The head of one of the panels has since written to one unsuccessful applicant (who with a similar proposal won DM265,000 from the Volkswagen Foundation) to say that a lottery would have been equally fair.

On the other side, the Ministry for Universities and Research claims that the



Seara — handing out

manifesto group is the naive political tool of the far Right, which wants to unseat the minister, Luis Gonzalez Seara, for his attempt to reduce professorial power with a bill now before parliament.

Seara's chief science adviser, sociologist Narciso Pizarro Ponce de la Torre, said at the Strasbourg meeting that his ministry (like Spanish democracy) was new and that the power of the Francoist professors was great, so that change had to be slow. Even so, the ministry is preparing a major policy statement, the 'livre blanc', on science for May 1981, together with a three-year plan that would multiply university research tenfold. But, said the manifesto group spokesman, the same has been said before, by three successive ministers: he will not believe it until it happens.

The seriousness of this conflict cannot easily be gauged. Narciso Pizarro accepts that a "more scientific" method has to be found for making the next allocation of grants. He is considering the appointment of international referees to some of the review panels for the next grant allocation in 1983. But he argues that the international community can itself be an inequitable power base for those with access to it, and wants to see a "just" distribution of funds. So does the manifesto group, although its wish that scientific excellence should be rewarded is seen as elitist in a fledgling democracy. The conflict is between the impatient and the gradualists.

Robert Walgate

US radioastronomy

Thinking big

San Francisco

Following the successful completion and inauguration of the Very Large Array (VLA) telescope in New Mexico last month, US radioastronomers are developing an ambitious scheme that would, in effect, turn the country into a single large radio telescope.

The VLA is designed to study relatively close objects whose distance from the Earth is of the order of thousands of light years. But to study the internal structure of quasars and the nuclei of galaxies the necessary resolution can only be achieved by the use of Very Long Baseline Interferometry (VLBI) in which data from several telescopes are combined to form a single image.

To some extent this can be done by linking existing telescopes, and since 1975 seven US radio telescopes have formed such an array. But there are several disadvantages, including the difficulty of coordinating and correlating data from machines designed and built for different purposes.

The new proposal, which has been developed by scientists from the California Institute of Technology (Caltech) and its Jet Propulsion Laboratory (JPL), is for a transcontinental array of ten 25-metre radio dishes, stretching from Massachusetts to Hawaii and controlled by a single central computer.

Such an array should provide an order of magnitude leap in the important parameters that could be measured compared with the data that can be collected from the present *ad hoc* arrangement. It could be used to provide fine detail radio maps of quasars and galaxy nuclei and also for making precise

measurements of the Earth's rotation, even providing information on plate tectonics.

The scientific and the economic feasibility of such a transcontinental array has now been demonstrated in a Caltech study which concludes that for extragalactic astronomy VLBI is the only tool available for detailed study of the energy sources in quasars and galaxies.

One feature of the Caltech proposal is that the array would be two-dimensional, with radio dishes as far north as Alaska. This spread will make it possible to cover almost all of the northern sky, in contrast to a Canadian proposal for a similar array with radio dishes essentially on a linear axis from Europe to British Columbia.

Two particular aspects of the array would improve performance compared with the present system. First, being able to locate the individual dishes in an optimal arrangement would make it possible to increase the dynamic range by an order of magnitude. This would allow detailed studies of the shape, size and evolution with time of the jets which are emitted from quasars and galaxy nuclei, in particular the acceleration and deceleration of so-called "knots" which occur within the jets.

The second advantage is that the array would be able to make measurements at frequencies of up to 15–20 GHz, considerably higher than some of the telescopes in the present array can achieve. This will make it possible to look much further down the jets to the surface of the objects from which they are emitted.

Radioastronomers in general are enthusiastic about the proposal for a ground-based array, which has been given top priority for funding in the next decade by the Field Committee responsible for overseeing research priorities in all fields of astronomy.

The main problem, inevitably, will be funding. The Caltech group estimates that the array will cost \$38.8 million, considerably less than other astronomical facilities (VLA, for example, cost \$80 million).

But astronomy, like other fields of basic science, is feeling the pinch. Already the National Science Foundation (NSF) has had to postpone plans for the next telescope on its priority list, a 25-metre dish that had originally been requested for funding in the fiscal year 1981 but failed to survive the budget review process.

There are three other schemes vying for funds. The National Aeronautics and Space Administration (NASA) has been working on plans for an advanced X-ray astronomical telescope, a successor to HEAO 2 and HEAO 3. In addition to the ground-based array, the NSF is already considering proposals for a 10–15-metre optical telescope, including designs that have been submitted by the University of California, the University of Arizona and the University of Texas.

Caltech scientists should have detailed plans ready for potential funding by 1982,

Any encounters, any kind

Voyager 1, now nearing Saturn, is far from innocent of messages to extraterrestrial civilizations (in which respect the article on page 9 is incorrect). Like its partner, Voyager 2, it carries a phonograph disk of copper (for long life) with sound recordings of greetings in 60 languages, a spoken message from Kurt Waldheim, Secretary-General of the United Nations, sounds of the Earth (natural, unnatural and musical) and a list of the members of the pre-election US Congress.

The disk also contains analogue tracks representing 100 photographs of the Earth and a message from President Jimmy Carter referring to "our progress towards a single global civilization" and "our wish to become a member of the galactic community". Voyager 1 was launched before the seizure of the US hostages in Iran.

and on such a schedule their array would be in operation by 1984–85. If the 25-metre dish is approved for funding next year, as hoped, there will be no conflict. However, if it is postponed again, then relations between what could become rival projects would be more delicate.

Experience has taught supporters of the ground-based array that any debate over who should run the facility ought to be resolved before the funding battle begins. Many feel that proposals for a mid-west telescope floundered because of inter-university rivalry for control. "We are determined not to make the same mistake again", says one radioastronomer.

David Dickson

Nuclear protests

Were Croats first?

With the Madrid Conference about to commence its review of the Helsinki Accords on Security and Cooperation in Europe and the Campaign for Nuclear Disarmament recently revitalized in the United Kingdom it is interesting to look back at what was almost certainly the first ever anti-nuclear protest — that of Dr Ivan Supek, a Yugoslav physicist, in 1944, more than a year before nuclear bombs were dropped on Hiroshima and Nagasaki.

Before the war, Supek had been a pupil of Heisenberg. In 1941, after a visit to

impossible the final victory of progressive forces — a victory which Marxist theory stated was inevitable. Therefore such weapons could not exist.

Supek, however, remained unconvinced, and a few months later published his papers from the congress in the Croatian popular science journal *Priroda* under the titles "Developments in Modern Physics" and "Science and Society".

Although at that time his main fear was of the perverted use that the Nazi regime could make of science (biology as well as physics), his stand against nuclear weapons has never wavered. He has from the beginning been an active participant in the Pugwash movement, and is extremely wary of proposals for peaceful uses of nuclear energy (including research), lest they be perverted to military ends.

Vera Rich

Research councils

Geological setback

The Department of the Environment will slash a third from its spending on geological science over the next three years, raising a question mark over the future of the Geological Survey of Great Britain, officials of the UK Natural Environment Research Council (NERC) said last week.

NERC was launching its first annual report since Sir Hermann Bondi took over a month ago as the new chairman of NERC (see *Nature* 5 June, p. 349). Bondi had no influence over the report and was much less concerned than his colleagues: "This report is not in my style", he said. "As you know, I'm an eternal optimist."

Bondi favours the Rothschild "customer-contractor" principle, which the report described as a threat. In 1973 NERC lost control of a third of its budget to government departments, following Lord Rothschild's recommendations for a shake-up in government science spending. At the time, the council warned that many of its projects — such as the Geological Survey — which were dependent on a group of customer departments would be vulnerable to the whim of any one of its customers. "It is of little comfort that this forecast is proving correct" says the report.

A quarter of NERC's £20 million contract research income depends on multi-customer contracts. The Geological Survey itself costs about £4.5 million a year, of which the Department of the Environment currently contributes £1.5 million. The survey was established in 1835, and produces near-surface and deep geological maps of Britain, improving them area by area as techniques develop. Some 180 scientist-years are spent each year on the survey, which involves 10 field units and a number of palaeontologists and chemists, mostly at the Institute of Geological Sciences (IGS).

The survey, UK geologists argue, is a national resource, drawn on regularly in

major civil engineering works, for example. But if the Department of the Environment takes too short a view, the value of the survey will be diluted and ultimately lost. A thorough survey for a "sheet" covering an area of 12 miles by 18 miles takes around 25 scientist-years and 5 to 7 years. "So you can't turn on a tap when you need a survey" said Dr Brian Kelk, who heads NERC's geosciences division. The survey is not purely an academic exercise. Dr Kelk argues that the survey must be developed on a continuous basis. It is not possible to predict exactly which areas are likely to prove important; for instance, the massive construction work carried out for North Sea oil terminals on the west coast of Scotland and the Shetlands would probably have been slowed without the geological maps which may have seemed of only academic interest when they were made in the 1920s.

Other bodies in the "consortium" which has managed the survey since Rothschild are the Department of Energy (contributing 5 per cent), the Department of Industry (also 5 per cent) and NERC (60 per cent, through the science vote of the Department of Education and Science). But the consortium will now collapse, with the Department of the Environment cutting its share to 20 per cent and offering its money piecemeal for particular areas and purposes. A new management structure must thus be found for the survey — and one is being sought actively by the director of the IGS, Dr G. M. Brown, who will present his proposals to NERC in two weeks' time. Dr Brown will also have to cope with other Department of the Environment cuts at IGS, where the department is reducing its spending from £3 million (at 1979 prices) this year to £2 million in 1982–83, out of a total IGS budget of £16 million. Staff recruitment, for one thing, will be reduced to a trickle.

Nevertheless, NERC's total income of £56.6 million in 1979–80 will hold roughly constant in real terms in 1980–81, largely through a slight increase in funds from the Department of Education and Science; but there is another problem over the replacement of the council's two research ships, RRS *Shackleton* and RRS *Discovery*. The *Shackleton* is older, and will probably be retired around 1983. The *Discovery* should remain effective until about 1987, but a new ship must be found to replace her if Britain is to maintain her place in oceanographic research, says NERC. This would cost £18–20 million at present prices, plus equipment: and to have her ready for the 1988 season, the order must be placed in 1984 at the latest. But there is no sign of the necessary money being made available — except perhaps if the ship were used jointly by the Science Research Council's Marine Technology Directorate and NERC.

It is here, perhaps, that Bondi's contacts and experience in the Advisory Board for the Research Councils — which advises on



Supek (left) and comrade, 1944

Heisenberg in Leipzig, he said that, although his main interest at the time was solid-state physics, he was able to make an "informed guess" that the Germans were working on both fission and fusion bombs.

Supek made his fears known in June 1944, at a congress of Croatian "cultural workers" (a term which included scientists) held in the newly liberated town of Topusko. His views did not go unchallenged. Several Marxist participants were doubtful that such weapons could exist at all. Nuclear weapons in Nazi hands, they argued, would render utterly

the science vote of the Department of Education and Science — may tell. He is reluctant to challenge the Rothschild principle, to which he still adheres firmly — while recognizing the dangers of multi-customer arrangements. He and his staff will redouble their efforts to get new contracts for support for projects in Third World countries. **Robert Walgate**

London university

Medical schools stay

Two of the medical school of the University of London, whose survival has been in doubt since March this year, were reprieved last Wednesday (29 October) by a resolution of the university Senate. The decision is regarded, within the university, as a sign that the more far-reaching inquiry into the organization of the university as a whole now under way will be less radical than some have feared.

The two medical schools concerned are Westminster Hospital Medical School and King's College Hospital Medical School (which includes a pre-clinical school at King's College proper and a clinical school at King's College Hospital, in south-east London). The disbandment of the two schools was recommended to the university in March by the report on medical teaching in the university prepared by a committee under Lord Flowers, rector of Imperial College.

The politics of last week's narrow Senate decision have a particular interest for the future reorganization of the University of London. The resolution eventually adopted by the Senate was proposed by Dr Bryan Thwaites, principal of Westfield College, one of the smaller institutions of the university. Thwaites and the others supporting the resolution argued that the university should not attempt to coerce constituent academic institutions into courses of action they found unpalatable.

This line of argument has an obvious bearing on the general inquiry into the organization of the university being conducted by a committee under Sir Peter Swinnerton-Dyer and set up by the vice-chancellor, Lord Annan, earlier this year. One possible outcome of that inquiry is a recommendation that the smaller institutions within the university might be merged with larger college or with each other. If however the principle of self-determination has been established, proposals involving loss of independence are less likely to be seriously put forward.

The battle over the independence of the two medical schools is not yet over. Although the decision may in principle be overturned by the Court of the university, this is unlikely without further consideration. A more likely course is that the Academic Planning Board, to which the issue has been referred, will come to a different decision from that of the Senate last week.

Séveso scare

Bloat, not poison

A flurry of fear last week that dioxin had reared its head again at Séveso has quickly abated. The local community was alarmed when 150 sheep died after spending a single night on a forbidden field, out of bounds to grazing animals for the past four years. The dead sheep were part of a flock of 250 driven 50 miles from the dry uplands of northern Italy.

First thoughts had blamed dioxin. The field was one of the most exposed when a chemical factory exploded at Séveso in 1976, distributing dioxin over the neighbourhood, and it had not yet been cleared for farming. (The shepherds say they did not see the notices.) But the sheep died too quickly for dioxin poisoning, and the levels in the field are now thought to be quite low. In fact the Séveso special office, headed by Senator Luigi Noé, was planning shortly to open nearby fields for cereal growing, but these plans were halted after the death of the sheep.

IMAGE
UNAVAILABLE
FOR
COPYRIGHT
REASONS

Dead sheep, dead landscape

However, the necropsies now show that the sheep died of bloat — severely distended gut, caused by the over rapid fermentation of wet hay, rye and grass in the stomachs of the hungry animals.

The result has been backed up by analysis of the livers of the dead sheep at the Mario Negri pharmacological research institute in Milan, which first detected dioxin in Séveso goats during 1976. According to Dr Luciano Manara, head of

the drug metabolism laboratory at the institute, the sheep had liver dioxin levels below 1 ng per g — compared with 1 µg per g in the most exposed goats in 1976.

Senator Noé has declared himself satisfied with these results, and has restarted the plans to open the Séveso fields. **Robert Walgate**

Bovine tuberculosis

Badgers at risk

Tuberculous badgers are more of a threat to themselves than to the cattle they infect. This is the nub of Lord Zuckerman's report on the British practice of gassing badgers, suspended a year ago after protests from conservationists (see *Nature* 28 October). Immediately after the publication of his report, *Badgers, cattle and tuberculosis* (HMSO, £5.20), the Secretary of State for Agriculture, Fisheries and Food announced that the practice of gassing infected badger setts is to be resumed as soon as possible and then reviewed after a three-year trial period.

Bovine tuberculosis is most common in south-west England, chiefly in the counties of Avon and Cornwall. The British badger population is to some extent concentrated in southern England, but the agriculture of the eastern counties is more concerned with cultivation than with cattle-rearing.

Evidence in the Zuckerman report for the association between bovine and badger tuberculosis is largely circumstantial. The incidence of bovine tuberculosis is correlated with that of badger tuberculosis and with the density of the badger population. There is also evidence that transmission from one species to the other is feasible. In Britain, the association (long suspected) became the basis for official policy on badger control only in 1971, after experience in New Zealand suggested that opossums were there a feral reservoir for bovine tuberculosis.

The issue has been contentious in Britain for the past decade. The Badger Act of 1973 gave badgers specific protection over and above the provisions of the Protection of Animals Act of 1911, but the Ministry of Agriculture was given power to control badgers (and even to enter farmers' land for that purpose) by later legislation in 1975 and 1976.

The causative organism of bovine tuberculosis, *Mycobacterium bovis*, is the chief cause of tuberculosis in badgers. The most arresting data in the Zuckerman report are those for the incidence of *M. bovis* infection in badgers. The most extensive series of measurements is that carried out by ministry laboratories of badger carcasses submitted for autopsy, usually after being killed on roads. In south-west England, more than 4 per cent of adventitious carcasses yielded *M. bovis*, while elsewhere in Britain isolation of the bacillus from dead badgers was sporadic and not statistically significant. In another

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survey of more than 4,000 badgers, 14 per cent were found to be infected.

The rate of badger infection on farms on which outbreaks of bovine tuberculosis have occurred is often much greater, approaching or even exceeding 50 per cent. The report says that the course of the disease among badgers is that of a virulent infection, with pups especially at risk.

In principle, there is no reason why wild animals other than badgers should not be infected with *M. bovis*, which has been found in small numbers of foxes, rats and moles. The Zuckerman report asks for a continuing survey of the occurrence of *M. bovis* and of other related bacilli, including *M. avium*, which has been found in deer, hares and hedgehogs, in particular.

Swedish Academy

Plugging Nobel gap

A Swedish industrialist, Dr Holger Crafoord, has given £500,000 — with more to come — to the Royal Swedish Academy of Sciences to institute a new series of scientific prizes in fields of science neglected by the Nobel awards — geosciences, biosciences (emphasizing ecology), mathematics with astronomy, and arthritis. The fund, called the Anna-Greta and Holger Crafoord Fund after Dr Crafoord and his wife, will amount to some £1 million by 1984 and the academy estimates it will yield interest of 13 per cent.

Only one third of the interest, perhaps £45,000 a year, will be spent on prizes. A quarter will go back to capital, and the rest

will go on research grants, to be awarded by international competition. The details of the award system are being worked out by a special commission, which will report to the academy early in 1981 in the hope that the first awards can be made that year. The intention is to avoid the season of the Nobel awards, traditionally made in late September and early October. There will probably be one prize in a single subject each year, rotating on a four-year cycle.

The subjects emphasized in the new award are the result of a few months' consultation between Crafoord and the academy. Dr Crafoord, who is general director of the biomedical firm Gambro AB of Lund, suffers from rheumatoid arthritis — hence the attention given to that disease.

Asked why he made the awards, Crafoord said last week "I had money enough!" Crafoord owns Gambro, which has some 20 per cent of the world market for kidney dialysis units. He felt he wanted to leave money to science, and asked the academy what fields were short of money. The allocation to research grants, as opposed to prizes, was made at his request. "I chose the academy because it was founded in the seventeenth century — it gives some guarantee that the fund will be maintained."

The academy does not see the awards as a chance to improve on the present system for the selection of Nobel prizewinners. "We are very happy with that" said an academy spokesman. "If we could match it for the new prizes we would be well pleased."

Robert Walgate

Brazilian biology

Humus from wood

A scheme for turning sawdust into humus, and exporting 600,000 tons of it to the Middle East, is being developed by Nutri-Humus Laboratories of Sao Paulo. This is the latest step in a long-term plan for liberating Brazilian agriculture from dependence on petro-dollars conceived by the bacteriologist Mario Nogueira de Oliveira, who founded Nutri-Humus 20 years ago.

The company began in a small way, supplying a few Brazilian farmers with the fermentation vessels, worms' eggs and organic fertilizers needed for the process. Now that rising oil prices are making the method economically competitive, and there is increased ecological consciousness, there is large-scale acceptance of the new approach.

On the farm, raw vegetable matter (sawdust, rice husks or bagasse from sugar cane) is spread over the fields at 10 to 20 tons per hectare, mixed with two 60-litre bags of pure humus and "earthworms' eggs" as a "primer", plus a third of a ton of natural phosphate obtained as a by-product of mining in the area. Next comes the novel part of the process — the land is sprayed with four types of brew, labelled enigmatically A, B, C and D.

Being something of an empiricist, and not wanting to release too many details of what might be a profitable enterprise, Nogueira does not explain his methods in full. But the additives include *Rhizobium* species bacteria such as *R. japonicum*, nitrogen-fixers and antifungal agents. It is claimed that the process manufactures organic fertilizer in 60 days instead of the usual 4 years at nature's own pace.

Industrially the plan is to use sawdust and wood chips which are the by-products of the timber industry of the Lages area of Santa Catarina state. The wood is hydrolysed with 0.3 per cent sulphuric acid before use and the exportable end-product is the "organic fertilizer", that is, 60-litre plastic bags containing the final humus breakdown products. This is now being made on fields in the Lages area and its market price is one-tenth that of chemical fertilizers in Brazil. It is hoped that a contract will soon be signed with the Libyan and Saudi governments for the sale of 200 shiploads of humus following the successful demonstration of alfalfa production on sandy terrain using Nutri-Humus.

Nogueira's long-term aim is self-reliance for Brazil's agriculture. He proposes a reduced cultivated area for sugar cane to serve as a generator of organic material. Each hectare of cane would fertilize 30 hectares of land in a year. As well as being freely available and high-yielding, sugar cane contains saccharose which facilitates the fermentations on which the Nutri-Humus process is based. **Maurice Bazin**

Franco-Soviet jaunt to Halley?

A joint Franco-Soviet mission to visit Halley's comet in 1985 has been announced. This comes as a surprise to many French astrophysicists, including those already involved in the European Space Agency (ESA) mission to the comet which, it seems, the Franco-Soviet experiment will to a large extent replicate. ESA officials confirmed that there is no possibility of France withdrawing from the European effort — participation is mandatory on all members.

France has always had a special relationship with the Soviet space programme. President de Gaulle was the first and so far the only Western leader to visit the Baikonur space centre. French participation in Soviet launches has included a laser experiment aboard the Lunokhod Moon-rover and a joint ionosphere experiment using high-altitude rockets launched from the Arctic and Antarctic ends of the same line of force. And two French cosmonaut candidates are now in training at the Gagarin space centre.

The propaganda value of these trainees, one of whom will become the first Western European to fly aboard a

Soviet spacecraft, has not been overlooked. At the beginning of October, Moscow radio commentator Boris Belitskii, after censuring the British media for neglecting the significance of the joint Soviet-Cuban flight, claimed that the training of the two French cosmonauts was even more "significant in terms of missed opportunity" for Britain. In the Soviet Union, he said, television viewers could watch cosmonauts carried aloft to work on a space programme geared to human needs, whereas in Britain the only rockets to appear on the television screens were American cruise missiles, plus, of course, science fiction epics.

Belitskii's message was clear — a Britain without US military missiles would be eligible for consideration as a future partner for the Soviet Union in space. He made no mention of the financial cost. Judging from the latest Franco-Soviet proposal, this need not be excessive in cosmic terms. The trip to Halley's comet — including the launching of French balloons above Venus — will cost France a mere 150 million francs (£15 million). **Vera Rich**

CORRESPONDENCE

Malaria vaccines?

SIR — Considerable effort is being directed towards producing a practical and effective vaccine against the most malignant human malaria, that caused by *Plasmodium falciparum*. The belief that this is feasible was based on the realization that human malaria induces effective specific immune responses which are protective. The best characterized of these are antibody-mediated, directed against stage and species specific antigens of sporozoites and merozoites and seem to act by preventing the entry of these two extracellular forms into their respective target cells, hepatocytes and erythrocytes.

However, the clinical effectiveness of natural immunity in exposed subjects is partially offset by processes generated by living plasmodia which permit evasion of immune effector mechanisms. These include the bewildering degree of antigenic diversity generated by the parasite as it differentiates through successive stages; also its ability to compromise host immunity through induction of immunosuppression and through polyclonal activation of lymphocytes and probably also by production of soluble antigen. Experimental vaccination with, for example, irradiated sporozoites or non-invasive merozoites, induces more effective immunity than does natural infection, indicating that nonviable forms of the parasite can stimulate protective immunity without activating processes favouring parasite survival.

The logical step from these observations is to develop stage-specific vaccines based on sporozoites and merozoites. The difficulty of obtaining these forms in sufficient quantities for even a restricted trial of adequately standardized material has encouraged detailed investigations into the structure of plasmodial antigens in the hope of identifying those involved in inducing protective immunity. This task was beset with technical difficulties, but the prospects have been transformed by the advent of techniques of somatic cell hybridization to generate cell lines which secrete monoclonal antibodies of defined specificity. The very first clone of antibody secreting cells raised against sporozoites led directly to the isolation of a stage-specific, surface-coat component of molecular weight 44,000 with the potential for promoting immunity to this clinically important stage of infection. With these specific probes it is becoming feasible to attempt the *in vitro* production through DNA cloning of plasmodial antigens having putative protective activity.

It is not surprising that such work should attract the attention of commercial interests, not least from those most recently founded and best equipped to exploit its potential. This intervention gives promise of greatly strengthening the malaria vaccine research effort, but some of its consequences may soon retard progress. Work on a malaria vaccine is unusual in requiring access to materials and facilities so diverse as to demand the collaboration of many laboratories. These requirements include a wide range of adequately characterized and geographically remote plasmodial species, their *in vitro* culture, the use of breeding colonies of

appropriate mosquito vectors, access to those few primate species susceptible to human malaria and eventually the organization of adequately controlled and locally acceptable clinical trials in countries which may have only rudimentary public health facilities. Despite these requirements some institutions are contemplating individually beneficial patent rights on segments of the work. This action already threatens to disrupt in part the complex web of collaborative work so central to success.

Malaria menaces over a third of the world's population and is confined almost exclusively to developing countries. There are around 150 million cases per year and over a million African children die annually of the disease. A recent intensive survey has shown that in the vast African savannah no known method of prophylaxis, however thoroughly dispensed, can in practice be effective. Elsewhere, for example in India and Sri-Lanka, it has proved impossible to sustain prophylactic measures and malaria is alarmingly resurgent. The cost of a developed malaria vaccine can never be recouped from the relatively impoverished countries which require it most urgently. Its manufacture and distribution will inevitably require massive subsidy from international governmental and charitable funds. Under these circumstances can any institution justify a claim to benefit individually from a restricted aspect of work, however important, which contributes to the development of a malaria vaccine? Procedural agreement is urgently required in this area of research. Representatives of major organizations involved should meet together forthwith under appropriate international auspices and agree a moratorium on all patent rights relating to the development of a human malaria vaccine. Is it really naive to believe that this enterprise cannot be sustained solely on the basis of its scientific feasibility and enormous practical potential for the health of mankind?

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Nobel Prize rules

SIR — Your editorial on changing the Nobel Prize rules (*Nature* 23 October, p.667) is right on all points. However, it does not mention one vital question — the statistics of sampling.

One way that the Nobel Foundation uses to select candidates is to write at random to about 50 universities for proposals. This list is different each year and comprises a sample of the about 900 universities around the globe (*Encyclopaedia Britannica*, *Micropaedia X*, pp.888-1007). As most of these universities are likely to have a chair in nuclear physics, but only about 10% one in spectroscopy, less than 10% in flow phenomena (hydro- and aerodynamics . . .); less than 5% atmospheric physics; less than 2% aerosol physics etc., the odds that a nuclear physicist will get the letter and nominate somebody within his own field, are incomparably greater than for any other branch of physics.

Proof: Between 1950 and 1973, 16 Nobel prizes went to some aspect of nuclear physics, 3 were awarded for low-temperature phenomena; 3 for optics; 2 for quantum

electrodynamics and 1 each for magnetism and semiconductors. Probably similar biases exist in chemistry and medicine.

In conclusion: the Nobel Prize goes by preference to the disciplines with the largest number of scientists. In other words, it is biased towards specialties best endowed with funds. This means that governmental budgeting interacts with the award.

It is surprising that such a select scientific body should not be aware of such a basic sampling error. More than a sampling error; this "pseudorandomization" goes against Nobel's will. At the end of the nineteenth century, physics was comprehensive and subdivision in specialties almost unheard of. Since then, electronics, atmospheric physics, rocketry, astrophysics and many, many other branches have become so detached, that scientists working in such areas are almost excluded from being considered for the prize.

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Fungal food

SIR — The recent article on fungal foods (*Nature* 4 September, p.6) states that the protein gap that was believed to exist in many developing countries has now been declared a myth. I have discussed a similar problem with Mr J. Todd, Executive Assistant to the Unitarian Service Committee of Canada — a Canadian charitable organization engaged in overseas relief and development in cooperation with governments of the least-developed countries. These countries are specifically chosen on the basis of a per capita income being less than \$200 per year. The agency is working in six such countries.

Mr Todd's description of the protein shortages in the many communities in which he works and the desperate need for protein in a wide variety of forms contrasts sharply with your statement. Although such countries are probably unable to buy protein from overseas, the lack of demand based on such inability can surely not be taken as an absence of need.

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ACHe uses

SIR — What, pray, is wrong with the determination of any government to attempt to protect its citizens, be they either soldiers or civilians, against the use of "nerve gas" (?organophosphorus) weapons? How can this be thought of as "distortion of technology"? R.G. Elles *et al.* (*Nature* 9 October, p.480) are adopting a stereotyped "holier than thou" attitude more appropriate to the behaviour of our "Praise-the-Lord Barebones" forebears of the post-Civil War period — "smelling-out" evils when they would be better occupied in haranguing protest meetings of a non-scientific nature; such letters are inappropriate for a science-based *Nature*.

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NEWS AND VIEWS

A close look at Saturn

from Philip Campbell

No photograph can do justice to what must surely be one of the most serenely beautiful sights in the solar system — Saturn and its ring system. Just over three years after launching, and having already revolutionized planetary studies with its exploration of Jupiter and its moons, Voyager 1 is about to begin the second exploration by spacecraft of Saturn — planet, rings and moons. The spacecraft's closest encounter will occur at 2345 GMT on 12 November at a distance of 124,200 km; the next two weeks, therefore, should provide a feast for astronomers and, no doubt, a fillip for NASA, troubled by escalating shuttle costs and by repeated budget cuts.

Voyager's encounter is the second of three. The first was by Pioneer 11, just over a year ago. Next August, Voyager 2, carrying similar instrumentation, will carry out a series of investigations complementary to those of Voyager 1. The trajectory of Voyager 1 has been designed to include a study of Titan, Saturn's largest moon, while the path of Voyager 2 is already set for Uranus and, it is hoped, Neptune. For that spacecraft, Saturn is, so to speak, an interesting view on the way. Voyager 1, on the other hand, will eventually pass out of the solar system without further known encounters — and without the hitherto obligatory message to exceedingly intelligent extraterrestrials.

Saturn's rings were first recognized by Huygens in 1656. From the earth, two rings can be seen most easily, rings A and B, separated by a gap known as Cassini's division. Following Pioneer 11, the number of distinct rings now known is five: in order of increasing orbital radius they are labelled C, B, A, F and E. Ring F is very narrow and was discovered by Pioneer 11, while ring E is wide and tenuous, extending from about 2.4 to 5 or 6 Saturn radii ($R_s \approx 60,000$ km) from the planet. (The existence of ring D, previously suggested by ground-based observations to be inside ring C, was not confirmed by Pioneer 11.) The number-density of particles varies considerably from ring to ring, but ground-based observations and an analysis of Pioneer 11's trajectory both indicate that the rings consist predominantly of low-density particles, covered with or consisting entirely of ices of H_2O and NH_3 . Moreover, ultraviolet measurements from the International Ultra-Violet Explorer

satellite and from Pioneer 11 have revealed that the rings are surrounded by an envelope of atomic hydrogen, possibly generated by photo-dissociation or the sputtering of the ice molecules.

Saturn's rings pose many problems. How did they form and evolve? Whether the rings originated in the tidal destruction of a moon or are a remnant of the proto-planetary nebula, several questions arise. Thus Cassini's division is known to occur close to the 2:1 orbital resonance of one of Saturn's smaller moons, Mimas. (That resonance is at the radial distance from Saturn at which a particle will orbit twice in the time it takes Mimas to orbit once.) One might expect a gap to appear at such a radius because the repetitive gravitational perturbation of Mimas would act so as to remove the particle from its orbit. But how is it that Mimas, only 350 km in diameter, can clear a division about 10,000 km in extent? And why is the division offset on the outward side of the Mimas resonance? Another question concerns the narrow F ring of Saturn — a question much stimulated by the discovery of other narrow ring systems around Jupiter and Uranus. A ring once formed should flatten and spread as a result of random collisions between the ring particles. Why has this not happened around Jupiter and Uranus? And why does the A ring of Saturn exhibit asymmetric spatial variations in brightness when viewed from the earth?

Whatever the answers to these questions — and several have been suggested over the past few years — they certainly involve interactions between the rings and Saturn's satellites. Two possible clues would be the discovery of moons orbiting within the ring system or the detection of density waves in the rings themselves*. The fact that spoke-like features have already been detected within the rings by Voyager 1 is a promise of things to come.

Voyager 1 is equipped for several different investigations of the rings. Apart from the two television cameras (which are sensitive enough to detect clumping within the rings but not individual particles), an infrared radiometer will be used to examine the brightness-temperature of particles as sensed in different relative positions of spacecraft, particle and the Sun, and also to monitor the rate at which the particles cool once they have entered the shadow of

Saturn. These measurements should yield particle sizes and compositions. An ultraviolet spectrometer will examine the hydrogen envelope of the rings. Finally, the spacecraft radio telemetry links will be monitored as the spacecraft, after the closest encounter, passes behind the planet and reappears behind the rings. Measurements of refraction and absorption of the radio waves by the rings should reveal details of the larger ring particles together with the overall ring thickness, known to be less than a few kilometres and possible only a few metres.

The body of Saturn itself will be investigated by the same techniques. Analysis of the spacecraft trajectory (monitored by the Doppler shift of the radio telemetry signals) will allow better values of Saturn's mass and gravitational moments to be calculated, enabling a density profile of Saturn's interior to be deduced. The post-Pioneer picture is of an oblate spheroid only 95 times heavier than the earth (although more than 800 times the volume) with one-fifth of the mass concentrated in a rocky core about twice the size of the earth. The core is thought to be surrounded by a layer of metallic hydrogen out to half the radius, beyond which is a gaseous envelope consisting predominantly of hydrogen and helium.

To refine this model, it is hoped that Voyager 1 will provide more details of Saturn's temperature structure and internal rotation. Pioneer 11 shed very little light on the question of rotation. Although the rotation period of the outer atmosphere is known to be about 11 hours, no indication was found of the inner rate. Had Saturn's magnetic field, discovered by Pioneer 11, been inclined to Saturn's axis of rotation, the internal period would have been easily determined. Unlike any other known planetary body, however, the magnetic field and rotation axes are aligned to within 1° . Voyagers 1 and 2 carry plasma and plasma wave detectors, magnetometers and radio receivers to investigate further the magnetic field and its interaction with the Solar Wind. (For a recent detailed discussion of the magnetosphere, see Cowley, *News and Views*, *Nature* **284**, 302; 1980.)

Visual observations of Saturn's atmosphere are greatly hampered by a thick ammonia haze, thought to be formed deep within the atmosphere but spread to considerable heights by convection. Cloud bands have been observed, and Pioneer 11 detected several features found on Jupiter

*Note added in proof: Two new satellites designated S13 and S14, have been discovered, one on either side of the narrow F ring. This may be consistent with a ring-confinement mechanism suggested by Goldreich and Tremaine (*Nature* **227**, 97; 1979).

to be characteristic of high wind shear. The much more sophisticated imaging cameras of the Voyagers, together with their facilities for detailed infrared and ultraviolet mapping and spectroscopy, should greatly improve understanding of the composition of the atmosphere and of its structural variations over the entire planet. At the time of writing, spot-like features have already been discovered.

The prospect of a close look at Saturn's moons must have the Voyager team salivating in anticipation. Will the outcome be as startling as that of the visit to Jupiter? The moons to be investigated are (in order of decreasing orbital radius) Iapetus, Titan, Rhea, Dione, Tethys, Enceladus

and Mimas. These bodies range in size from 175 km (Mimas) to 800 km (Iapetus), Titan standing out at 2,915 km. They will all be mapped optically and scanned in the infrared and ultraviolet to determine surface temperatures and to detect possible gaseous emissions in molecular, atomic or ionized form. The infrared radiometer will also observe an eclipse of Rhea by Saturn; the cooling should provide some clue to the thermal properties and structure of the satellite's surface.

Titan is, as far as is known, alone among Saturn's moons in possessing a substantial atmosphere. No surface features have yet been detected. Ground-based observations do however suggest that Titan's reflec-

tivity, contrary to what would be expected from a gaseous atmosphere, decreases with increasing frequency, so that Titan appears reddish in colour: this has been interpreted as a manifestation of a high-altitude aerosol layer. On the structure and composition of the atmosphere of Titan, it is agreed that methane, ethylene and ethane are present, and Pioneer 11's ultraviolet instrument detected an extensive atomic hydrogen cloud surrounding Titan and possibly extending around part or all of its orbit. The presence of nitrogen in the atmosphere is a source of controversy. Voyager 1, approaching within 4,000 km of Titan, should certainly resolve these problems. No doubt it will throw up many more. □

How much genetic variation?

from J. S. Jones

WITHOUT genetic variation, evolution cannot take place. The measurement of the extent of polymorphism is hence a prime task for evolutionary biologists, and a variety of genetic and biochemical techniques have been used to this end. Brown¹ has recently found extensive genetic polymorphism in the mitochondrial DNA of man by using a restriction endonuclease analysis which detects individual differences in the DNA sites susceptible to enzyme degradation. Similar polymorphisms exist in human nuclear DNA². Although the study of polymorphism in the structure of the DNA itself is likely to be a time-consuming affair, improvements in the methods available for the study of proteins have already greatly altered our view of genetic variation at the level of the gene product. This new information has important implications for evolutionary theory.

Gel electrophoresis, which utilizes the migration of proteins in an electric field to detect small differences in their charge and shape, can be used to estimate the proportion of a randomly chosen sample of gene loci which is polymorphic. Simple one-dimensional electrophoresis of a sample of loci coding for soluble enzymes was first carried out about fifteen years ago using *Drosophila pseudoobscura* and many organisms have now been surveyed³. In general it seems that about a quarter of the loci tested show genetic variation. Most polymorphic loci have rather few alleles; two or three is the norm although there are occasional loci with up to ten.

The unexpected discovery of widespread genetic variation led to a controversy as to whether protein polymorphism is actively promoted by natural selection, or whether it is largely 'genetic garbage' without much evolutionary relevance. Biochemists and

some theoretical biologists have tended to emphasize the importance of selection, but a number of widely discussed mathematical models incline towards the latter view⁴. In general, theories of the selective maintenance of molecular polymorphism find it difficult to accommodate very large amounts of variation, as such theories depend on, for example, differences in fitness between heterozygotes and homozygotes, or differences in the ability of the various alleles to survive in different ecological niches. As the amount of polymorphism increases, these differences must become vanishingly small. Theories of selective neutrality, however, depend largely on two parameters, one of which (the mutation rate) is very small, while the other (population size) may be very large. Both are difficult to measure, but it is clear that, at least in organisms with large populations (such as *Drosophila*), the neutral theory must predict that while many loci might be invariant, others should have very many alleles. The electrophoretic techniques used until recently, however, have demonstrated a rather limited range of variation over different gene loci and have also shown that the majority of enzyme polymorphisms have rather few alleles. Also, according to a theory of selective neutrality of protein polymorphism, closely related species (which share a common ancestor but which have been unable to exchange genes for many generations) are expected to accumulate a different series of alleles because of the action of a different set of random processes over time. This does not seem to be the case; in *D. pseudoobscura*'s sibling species *D. persimilis*, nearly 90 per cent of the polymorphisms detected by simple electrophoresis show identical patterns of genetic variation, although the last gene interchange between these species occurred several million generations ago⁵.

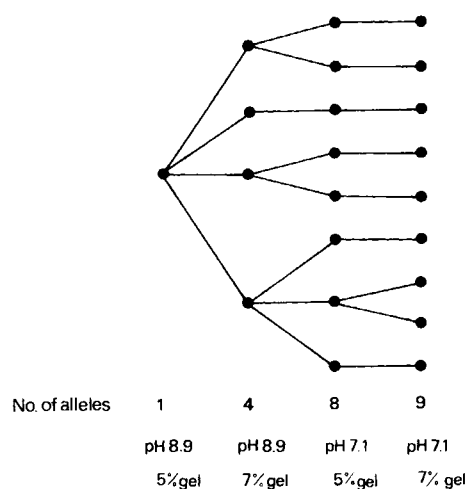
These observations led many biologists

to believe that molecular polymorphism must be actively maintained by natural selection, although the details of the process remained obscure. However, new improvements in the technique of electrophoresis have led to a renewal of support for the theory of selective neutrality. First (as recently discussed by Edwards and Hopkinson⁶) most speculation has been based on data from a very biased sample of gene loci, which ignores structural proteins in favour of genes coding for soluble enzymes. Structural proteins are the most abundant molecules in the cell. Use of the very sensitive new technique of isoelectric focusing in one direction, followed by electrophoresis of the molecules dispersed through the gel at right angles to the focusing path (a method which can detect single charge changes), shows that structural proteins have almost no genetic polymorphism. Estimates of genetic diversity based only on a small sample of enzyme loci are therefore very misleading. In addition, there are serious limitations in the techniques used in enzyme electrophoresis. It has always been accepted that electrophoresis cannot detect all amino acid substitutions. Electrophoretically homogeneous classes of *Drosophila* enzymes are genetically variable in, for example, their resistance to heat treatment and in their ability to form dimers^{7,8}. However, only in the last three years has it been realized just how weak the traditional methods of gel electrophoresis may be in detecting enzyme polymorphisms.

Singh, Lewontin and Felton⁹ describe some inelegant but practical developments of this technique which they have used to detect new enzyme polymorphisms in *D. pseudoobscura*. They worked first on the xanthine dehydrogenase (*Xdh*) locus. Simple electrophoresis at pH 8.9 on a 5% polyacrylamide gel had revealed only six alleles at this locus. However, sequential analysis of apparently homogeneous

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Fig. 1 Sequential analysis of an apparently homogeneous xanthine dehydrogenase allele in *Drosophila pseudoobscura*. In all the inbred lines studied, six alleles were revealed in the first set of electrophoretic conditions. After each of the lines were examined on gels of 7% concentration (rather than 5%), 13 variants were discovered. Further examination of these on a 5% gel at pH 7.1 revealed 11 more alleles, and subsequent analysis on a 7% gel at this pH gave 27 genetically different forms. Ten further alleles were distinguished by studying inherited differences in the enzyme's heat stability. Sequential analysis increases the amount of polymorphism detected by six times.



inbred lines on gels of different concentration and pH revealed many previously undetected alleles (Fig. 1). This technique distinguishes 37 alleles, instead of the six previously detected. As only 146 genomes from nature were examined, the total number of alleles at the *Xdh* locus may be even greater.

Sequential electrophoresis does seem to detect most amino acid substitutions. The complete amino acid sequence of many mutant haemoglobins is known; one-step electrophoresis lumps together these different haemoglobins into a series of genetically heterogeneous classes¹⁰. However, sequential electrophoresis allowed 17 of 20 mutant haemoglobins¹¹ to be distinguished. This method has now been used on several enzyme systems in *D. pseudoobscura* and *D. melanogaster*¹²⁻¹⁵. Some, but not all, loci have shown a great increase in the extent of their genetic polymorphism. The locus coding for aldehyde oxidase, which was previously thought to have very little genetic variation, is now revealed to possess 16 alleles, while that for esterase-5 increases from 13 to 32. Hexokinase-1 and octanol dehydrogenase show almost no increase in the number of alleles when the new methods are applied. There are no obvious associations between the extent of this newly discovered polymorphism and the enzyme's molecular weight or biochemical function.

These improvements in technique have greatly altered our view of molecular polymorphism. On the one hand there exists a class of structural proteins which are almost invariable, while on the other at least some soluble enzymes show a very high level of genetic variation. This observation accords well with the latest predictions of theoreticians who feel that most molecular polymorphism is not actively favoured by natural selection. The recent models of Kimura¹⁶ and of Ohta¹⁷ incorporate weak natural selection acting against slightly deleterious mutations but

suggest that most mutants have almost no effect on the fitness of their carriers. Structural proteins are highly invariant as they are closely interlocked with each other and have a low tolerance to mutations which change their shape. Any mutants are removed by natural selection. Membrane-bound enzymes are also quite dependent on accurate steric relations with other molecules in the membrane and can thus tolerate only a small amount of polymorphism. Soluble enzymes such as xanthine dehydrogenase, however, are subject to few such constraints; most of the changes in amino acid sequence which result from mutation have no effect on the molecule's function and persist for a period which depends only on the accidents of sampling. Animals which maintain large populations will accumulate very many alleles at such loci, and there is no need to argue that each protein polymorphism is actively maintained because of its biologically useful role.

On previous estimates, *D. pseudoobscura*'s sibling species *D. persimilis* appeared to possess three *Xdh* alleles, two of which were shared with *D. pseudoobscura*⁵. Their close resemblance had been used to suggest that the polymorphism was conserved by natural selection even after speciation. However, when this locus was examined using sequential electrophoresis, 23 alleles were found in a sample of 60 *D. persimilis* genomes¹⁸. Only three of these are shared with *D. pseudoobscura*, and only one is at all common in both species. The two species, although closely related, have therefore diverged almost completely at this locus since gene exchange was interrupted by speciation. It seems more reasonable to interpret this difference as resulting from a balance between the random origin and extinction of selectively equivalent alleles within each species than to postulate that *pseudoobscura* and *persimilis* (which often occur in the same place) are subject to a completely different set of selective forces.

The existence of the patterns of genetic variation discussed here is not in itself a proof that natural selection is unimportant in maintaining molecular polymorphism. There is experimental evidence for differences in the fitness of electrophoretic alleles at some enzyme loci¹⁹⁻²¹ and it is possible that even the dozens of alleles now known to exist may each be found to respond to natural selection, or that new theoretical treatments will show how such extensive polymorphism may be selectively maintained. However, the new data on molecular polymorphism and the cloning a polymorphic enzyme locus in *D. pseudoobscura* into *Escherichia coli*²² (which may enable large quantities of purified enzyme protein to be produced for further analysis of hidden genetic variation) show that — as so often before in the study of evolution — the experimental cat is among the theoretical pigeons. □

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Flat-spectrum radio sources: victims of a conspiracy?

from Alan P. Marscher

In early surveys of the radio sky, taken at wavelengths in the 100-metre range, radio astronomers found that most extragalactic radio sources appear very similar to one another. These objects, identified with radio galaxies and quasars, exhibit spectra which have steep negative slopes, that is the radio flux decreases sharply with increasing frequency. However, later surveys performed at centimetre wavelengths yielded a large number of so-called 'centimetre-excess' objects whose spectral slopes are positive, zero, or undulating. K. I. Kellermann and I. I. K. Pauliny-Toth (*Astrophys. J. Lett.* **155**, L71; 1969) interpreted this to be the result of a superposition of several discrete, compact components, each of which exhibits a turnover in its spectrum at a given wavelength below which the synchrotron emission is self-absorbed. Subsequent observations with very-long-baseline interferometers (VLBI) confirmed that these centimetre-excess sources are indeed very compact, with angular sizes often smaller than 0.001 arc s.

The difficulty with the superposition hypothesis lies in the large number of radio sources whose spectra are both quite flat and rather smooth. A random distribution of several self-absorbed components should yield a much larger percentage of undulating spectra than are observed (D. B. Cook & S. R. Spangler *Astrophys. J.*; in the press). This situation has led several authors to suggest that the flat-spectrum sources are produced by a single component whose magnetic field and relativistic electron density decrease with distance from the centre. In this way, a single, inhomogeneous component mimics the spectrum emitted by an infinite distribution of concentric, uniform components and produces a smooth, flat

spectrum (J. J. Condon & L. L. Dressell *Astrophys. Lett.* **15**, 203; 1973).

One such flat-spectrum radio source, the BL Lacertae object PKS0735 + 178, was suggested by A. P. Marscher (*Astr. J.* **82**, 781; 1977) to be a prime candidate for a study to determine which point of view is correct. Its radio spectrum in 1977 was, to within observational errors, perfectly flat over more than two decades of frequency. It was suggested that multi-wavelength VLBI observations would allow one to differentiate between models involving multiple, uniform components and those invoking a single, tapered component.

Several groups have performed these critical observations, and the results are now being published. W. D. Cotton *et al.* (*Astrophys. J. Lett.* **238** L123; 1980) have obtained VLBI observations of PKS 0735 + 178 at four wavelengths — 2.8, 3.7, 11–13 and 50 cm. Although their data at any given wavelength are rather limited, they do, in fact, clearly indicate that this radio source is composed of several distinct, compact components, in line with the superposition hypothesis of Kellermann and Pauliny-Toth. Other observers have obtained more detailed data at various frequencies, with a general picture of the source which basically agrees with the Cotton *et al.* interpretation (A. P. Marscher & D. B. Shaffer *Astr. J.* **85**, 668; 1980; L. B. Bååth *et al. Astr. Astrophys.*; in the press). Of particular interest are the detailed 6-cm observations of Bååth *et al.* (see Fig. 1). These authors find that the structure of PKS0735 + 178 is rather complex, consisting of two compact components plus a more diffuse, jet-like feature extending past the weaker hotspot. In addition, there is a weak, even more diffuse, resolved emission region. Thus, as Cotton *et al.* remarked, this flat-spectrum

radio source seems to be the result of a 'cosmic conspiracy' of several compact components which, when superposed, manage to produce a smoothly varying, flat spectrum.

An important clue to the resolution of this conspiracy might lie in the remarkable similarity in appearance of the radio maps of PKS 0735 + 178 and the two well studied objects 3C273 and 3C345 (A. C. S. Readhead *et al. Astrophys. J.* **231**, 299; 1979). All three sources contain a bright, unresolved component, with a jet-like feature emanating to one side of this hotspot, plus one or more 'knots' of enhanced emission embedded in the jet. R. D. Blandford and A. Königl (*Astrophys. J.* **232**, 24; 1979) have interpreted the bright, unresolved component to be the narrow end of a synchrotron-emitting plasma beam, the fluid in which is moving relativistically. The more diffuse jet is then just the fanned-out extension of this beam (which we are viewing nearly end-on, since this configuration enhances the brightness, making such a source more likely to appear in a flux-limited survey of radio sources). The secondary knots are formed through either some instability in the beam or interaction with cooler gas which the beam encounters. If this picture is correct, one would expect all of the components to be physically associated, having been created one way or another by the relativistic beam. The beam itself is smoothly inhomogeneous, with density and magnetic field strength decreasing as the beam widens. Components appearing downstream might then be related by some simple scaling law to those observed upstream. The beam might thus be capable of modulating the physical parameters of the various components in the source such that they 'conspire' to emit a smooth, flat radio spectrum.

Since the beam is smoothly inhomogeneous, the size of the component at its narrow end should appear to increase with wavelength (see A. G. de Bruyn *Astr. Astrophys.* **52**, 439; 1976; A. P. Marscher *Astrophys. J.* **216**, 244; 1977). This should cause the separation between the bright, unresolved hotspot and secondary knots to decrease somewhat with wavelength. Further detailed multi-wavelength VLBI observations should be capable of determining whether this is, in fact, the case, and thereby test the model.

Finally, it is worthwhile noting that the two objects whose radio structures closely resemble PKS0735 + 178, 3C273 and 3C345, both exhibit rapid changes in the separation of their components. If the distances to these quasars are determined through a cosmological interpretation of the optical redshifts, using a standard

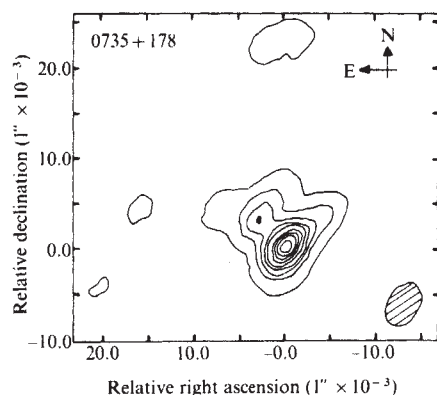


Fig. 1 Radio map at 6 cm of the compact core of PKS0735 + 178. Easily spotted on the map are the bright, unresolved component, the secondary, compact knot to the north-east, and the more diffuse jet, also extending to the north-east. The larger, diffuse component is resolved out on this scale and hence does not appear. From Bååth *et al.* (*Astr. Astrophys.*; in the press).

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Friedmann cosmology, the observed angular velocities of separation correspond to speeds far in excess of the speed of light (see M. H. Cohen *et al.* *Nature* 268, 405; 1977). The relativistic beam model mentioned above can explain this phenomenon as a consequence of shortened observed arrival intervals of successively emitted wave fronts. This is caused by the motion of the emitting plasma, which approaches

the observer almost as rapidly as do the radio waves (see M. J. Rees *Nature* 211, 468; 1966). From the above discussion, one can therefore predict that PKS0735 + 178 should also be engaged in such 'superluminal' expansion. Further VLBI monitoring of this source should allow radio astronomers to test this prediction and thereby increase our understanding of compact radio sources. □

microfilament and membrane in such an assembly. However, research moves so quickly in this field that, already, several refinements are required of this model. α -actinin does not seem to occur sufficiently close to the dense plaque of epithelial *zonulae adherentes* junctions for it to be the mediator of actin's linkage to the membrane (Geiger *et al.* *Proc. natn. Acad. Sci. U.S.A.* 76, 2833; 1979). Further work is required to define its location as it is detected within analogous focal adhesion plaques isolated from the cell body (Badley *et al.* *Expl Cell Res.* 117, 231; 1978; Rohrschneider & Shriver *Eur. J. Cell Biol.* 22, 521; 1980). The current view seems to be that α -actinin collects actin microfilaments laterally to form bundles — a function also tentatively assigned to a new 130 K protein first found as a contaminant in preparations of gizzard α -actinin. When used to stain cultured chicken cells, antibodies raised against this protein (Geiger *Cell* 18, 143; 1979) produce a punctate pattern at the ventral surface. These sites turn out to be focal adhesion plaques and Geiger concludes that "the 130 K protein plays a more direct role than either α -actinin or tropomyosin in the association of actin filaments with the cell membrane". In addition, the protein has been shown to terminate microfilament

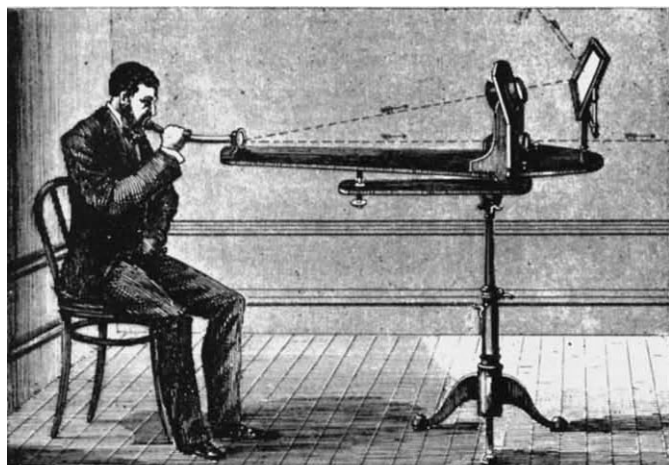
Hot foot

from Clive Lloyd

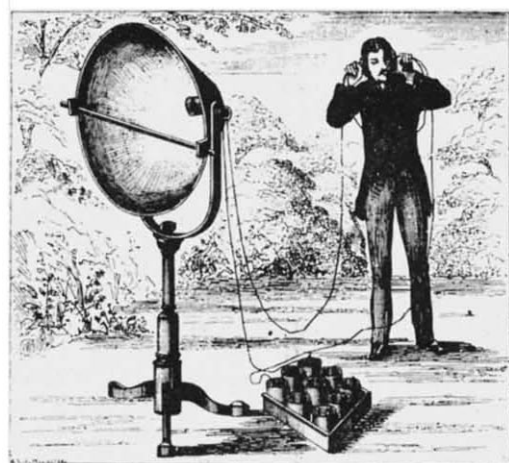
CONSIDERING its location at the boundary between cell and environment, it is not surprising that the fibroblast's focal adhesion plaque or 'foot' has become a fashionable meeting point for a whole gaggle of animal cell biologists. The reasons for investigating the foot by interference reflection microscopy are diverse — the study of microfilament bundle attachment, cell locomotion,

morphology and virus infection — but in coming together at this site, these studies raise universal issues of cell behaviour and growth control.

In a previous article (News & Views *Nature* 279, 473; 1979), it was reported that extracellular fibronectin and cytoplasmic microfilament bundles had been seen to be co-linear across the membrane suggesting that α -actinin provided the linkage between



The articulating photophone. The transmitter.



The selenium receiver.

100 years ago

BELL'S PHOTOPHONE

By the courtesy of Prof. Graham Bell we are at length able to do somewhat ampler justice to his latest discovery than has hitherto been possible. He has supplied us with certain details not hitherto published, and has also furnished us with drawings of his apparatus and experiments.

Our readers are already aware that the object of the photophone is the transmission of sounds both musical and vocal to a distance by the agency of a beam of light of varying intensity; and that the first successful attempts made by Prof. Bell and his co-labourer, Mr. Sumner Tainter, were based upon the known property of the element selenium, the electric resistance of which varies with the degree of illumination to

which it is exposed. Hence, given a transmitting instrument such as a flexible mirror by which the vibrations of a sound could throw into vibration a beam of light, a receiver consisting of sensitive selenium forming part of an electric circuit with a battery and a telephone should suffice to translate the varying intensities of light into corresponding varying intensities of electric current, and finally into vibrations of the telephone disk audible once more as *sound*. This fundamental conception dates from 1878, when in lecturing before the Royal Institution Prof. Bell announced the possibility of hearing a shadow fall upon a piece of selenium included in a telephone circuit. The photophone, however, outgrew the particular electrical combination that suggested it; for not the least of the remarkable points in this research is the discovery that audible vibrations are set up in thin disks of almost every kind of material by merely throwing upon them an intermittent

light. Hence in theory, if not in practice, the receiver may be reduced to the divine simplicity of a mere disk of vulcanite or of zinc; on one side of which the listener listens.

We may classify the forms of photophone under two heads, as (1) articulating photophones, and (2) musical photophones; the former being able to transmit speech because they work by beams of light whose intensity can vary in undulatory fluctuations, like those of vocal tones; the latter being able to transmit simple musical tones only, since they work by mere interruptions of a fixed beam of light. The greatest distance to which articulate speech has yet been transmitted by the selenium-cell-photophone is 213 metres, or 233 yards.

Whatever be the future before the photophone, it assuredly deserves to rank in estimation beside the now familiar names of the telephone and the phonograph. From *Nature* 23, 4 November, 15, 1880.

bundles (in a study which suggests a relationship between the 130 K protein, fibronectin and microfilament bundles, Burridge & Feramisco *Cell* **19**, 587; 1980), and is found at three varieties of tissue junction (Geiger *et al. Proc. natn. Acad. Sci. U.S.A.* **77**, 4127; 1980) and at broad areas of close contact between cultured rat myotubes and glass coverslips (Bloch & Geiger *Cell* **21**, 25; 1980). Its characteristics do not, however, suggest it to be of the integral type which could span the membrane. In fact, it is reported to be virtually nonexistent in isolated HeLa plasma membranes which do contain actin (Burridge & Feramisco *Eur. J. Cell Biol.* **22**, 350; 1980) — properties which hint at a role for the 130 K protein in consolidating microfilaments into bundles rather than linking them to membranes.

This leaves open the question of what actually links actin to the membrane. There are doubts, too, about whether fibronectin is the extracellular limb of the transmembranous assembly. EM sections had shown that actin microfilaments and fibronectin fibrils are co-linear and come very close to touching across the membrane (Hynes & Destree *Cell* **15**, 875; 1978; Singer *Cell* **15**, 675; 1979). Fibronectin is also found to be concentrated at isolated feet (Badley *et al. Expl Cell Res.* **117**, 231; 1978). Now, by taking double exposures of immunofluorescence (to reveal fibronectin) and interference reflection (to reveal focal adhesion plaques), Birchmeier *et al. (Proc. natn. Acad. Sci. U.S.A.* **77**, 4108; 1980) demonstrate that fibronectin is absent from the foot. Geiger reports a similar conclusion (*Eur. J. Cell Biol.* **22**, 350; 1980). An obvious distinction can be made between the techniques that have localized fibronectin at the foot and those that have not — the former either slice or isolate the target site whereas the latter rely on the ability of antibodies to penetrate stable adhesion plaques borne upon whole cells. Questions of accessibility are bound to be prominent in the coming debate.

In attempting to dissect the molecular anatomy of cell/substratum interactions, there is a natural preoccupation with the foot and its attendant musculature but this is not the only relationship that a cell strikes with the substratum. Fibroblasts which migrate out from pieces of embryonic chick heart are highly motile but this locomotion is based on the formation of the broad, unfocused and transient close contacts which are associated with a diffuse actin meshwork (Couchman & Rees *J. Cell Sci.* **39**, 149; 1979; see also, Abercrombie *et al. Expl Cell Res.* **67**, 359; 1971; Badley *et al. J. Muscle Res. & Cell Motility* **1**, 5; 1980). It is some time later (24–48 h) that the migrating cells become stationary and form the more stable focal adhesion plaques which terminate stress fibres. This conversion from the motile to the sessile condition also coincides with a metamorphosis from polarized to polygonal shapes, a greater abundance of fibronectin and exit

from post-mitotic arrest into the division cycle. Microfilament bundles and feet are therefore not essential for motility and the suggestion is that they set-up cells for anchorage-dependent growth rather than to facilitate movement. This agrees with findings that anchorage-dependent mouse fibroblasts, which had been maintained in suspension, require to re-attach and spread in order to restore DNA synthesis, rRNA synthesis and mRNA production, whereas attachment alone restores only protein synthesis (Ben-Ze'ev *et al. Cell* **21**, 365; 1980).

Observations such as these touch a nerve that runs through much of the fascination with the cytoskeleton: that the way in which it is organized relates to the state of cell growth. It is precisely here that the *src* gene could prove to be an effective probe by disentangling growth control from contact behaviour. This gene of Rous sarcoma virus is responsible for transforming the morphology, motility, metabolism and growth regulation of avian and mammalian cells (Hanafusa in *Comprehensive Virology* **10**, 401, eds Fraenkel-Conrat & Wagner, Plenum, New York; 1977). In order to understand this cluster of responses, it is clearly important to determine the gene product's site of action. That a target for the *src* gene product is the cytoskeleton was suggested by McClain *et al. (Proc. natn. Acad. Sci. U.S.A.* **75**, 2750; 1978) on the basis that dissolution of microfilament bundles occurred within 30 minutes of the microinjection of cytoplasmic extract derived from virus-infected cells. The gene product is now known to be a 60,000 dalton phosphoprotein — a kinase termed pp60^{src} which phosphorylates proteins at tyrosine (see Hunter & Sefton *Proc. natn. Acad. Sci. U.S.A.* **77**, 1311; 1980). From its recently determined nucleotide sequence and its association characteristics with plasma membrane preparations (respectively, Czernilofsky *et al. Nature* **287**, 198; 1980; Courtneidge *et al. Proc. natn. Acad. Sci. U.S.A.* **77**, 3783; 1980), it is believed to be embedded in the membrane with its protein kinase activity accessible at the cytoplasmic face. In the light of this, its detection (Rohrschneider *Proc. natn. Acad. Sci. U.S.A.* **77**, 3514; 1980; see Fig. 1) at focal adhesion plaques is highly intriguing since its occurrence there places it at the heart of the adhesion/motility/morphology syndrome. With anti-serum specific to pp60^{src}, Rohrschneider detected a speckled pattern of staining on the ventral surface of RSV-transformed rat kidney cells — a pattern which coincided exactly with the distribution of feet (and not with the broader close contacts). The protein kinase was also found in isolated focal adhesion plaques but only from cells infected with the temperature-sensitive mutant when maintained at the permissive temperature; not from cells maintained at the non-permissive temperature at which infected cells appear normal. Since the focal adhesion plaque itself (as distinct from associated microfilament bundles) is formed at both permissive and non-permissive temperatures, it would appear that the protein kinase does not affect foot formation *per se* but perhaps some microfilament-based activity such as their ability to pack into bundles.

A preliminary report provides an interesting postscript to this by suggesting that within adhesion plaques and cell-cell junctions “pp 60^{src} was closely associated with actin, α -actinin and a 130 K protein” (Rohrschneider & Shriver *Eur. J. Cell Biol.* **22**, 521; 1980).

Perhaps further studies on the foot will help nail the persistent idea that cytoskeletal organization and cell growth share something in common. □

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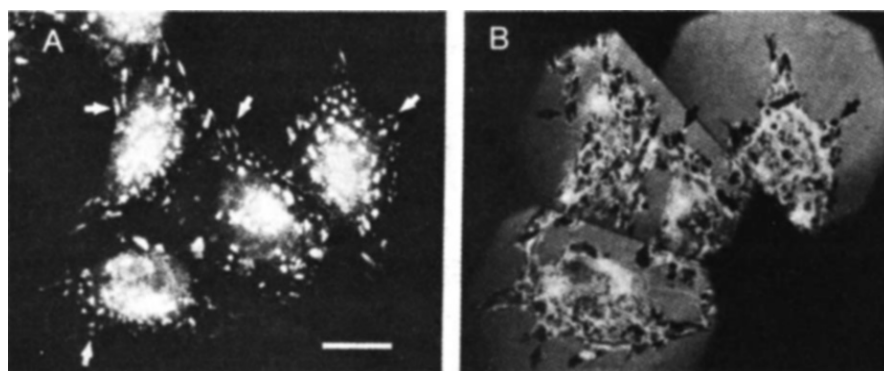


Fig. 1 Comparison of the same NRK cells by immunofluorescence for pp60^{src} (A) and interference reflection microscopy (B) demonstrating that the *src* gene product is localized at focal adhesion plaques.

AUTUMN BOOKS SUPPLEMENT

Microprocessors and the printed word

There is now a chance that the coming decade will see the flowering of the revolution in communications that the prophets of technology have foretold since the end of the Second World War. Microprocessors, distributed computer facilities and the like offer powerful ways of storing and handling information. Novel kinds of communications channels promise widespread access, flexibility and low cost. Means of turning electronic representations of information into forms that can be read by human eyes and processed by human nervous systems become more versatile as the years go by. The chances that these devices will be welded fruitfully together in the 1980s are greater than in previous decades. It is, of course, far too soon to be certain how the decade will turn out. A severe and probably prolonged economic recession throughout the industrialized West is hardly the best time for launching a major revolution of technology. Lack of capital may yet frustrate the plans being laid for the new communications technology. Yet it is only prudent that people should be asking what will be the consequences of the promised changes. Already there is a vigorous if somewhat shapeless debate about the consequences for employment: will there be more of it, or less? That argument is likely to grumble on, unresolved, for many years to come. What of more specific questions such as the consequences of the new technology for communication in science and technology? In particular, are the days of the conventional journals numbered?

This is one of the questions raised by a study, now published, carried out by the Primary Communications Research Centre at the University of Leicester. (*New technology and developments in the communication of research during the 1980s*, obtainable from the centre at £2.50 within the UK, £3.00 elsewhere.) For what it is worth, the report of the study appears on ordinary paper. The type has been set by pointing cameras at sheets of typewritten paper. Distribution is conventional, by post. Clearly those who pave the way for revolutions must conduct themselves conventionally for a time, as John the Baptist discovered to his cost.

Indeed, the report of the Leicester group, led by Professor Jack Meadows, is largely a sketch of what the future may bring in the communication of information in science and technology. It is a survey of the options that may open up, not a prescription for a preferred course of development. That, too, is seemly. For in the end, the ways in which scientists communicate with each other will be determined by what they want to do.

It is not, however, too soon to think of what the future may be like. The most radical revolution of the scientific literature rejoices in the name of the "electronic journal". The idea is simple. Somewhere there is a computer system capable of storing scientific articles together with the data, in tabular form, as graphs and photographs. People wishing to submit articles for "publication" merely arrange that the text of their contribution is fed into the system. At some stage, human editors must intervene, if only to decide which scientists in which laboratories should be invited to referee which articles, but from that point the process of publication is more or less mechanical. Referees' comments come and go by the same communications system. Authors are invited to amend their manuscripts, and the revised versions are in due course listed in the public file of articles to which all and sundry may have access. Reading a journal will then be simply a process of pressing an appropriate button on a communications terminal to summon up the latest table of contents and then to display whatever articles may be of particular interest.

This version of the future has a number of attractive features. In principle, it is capable of great flexibility. Some readers of some

electronic journals might wish to read the abstracts of all the articles on the file, and could no doubt be satisfied by pressing a few extra buttons – and for an extra charge. The editors of some journals might decide that articles should be available on the network before they have been refereed, so that readers could share with authors the experience of seeing articles take their final form. Some visionaries even dream of schemes in which the whole of some group of interested specialists would be involved in the assessment of each individual's contributions to the literature. The result might be a much greater sense of community, and that the literature of some field of research is truly the collective understanding and the common heritage of those working in it. Such schemes are by no means as fanciful as they sound. Some of the more interesting of the journals in the conventional scientific literature are those in which each article is accompanied by a string of written comments from others with useful things to say about them.

More modest benefits of electronic journals are probably more nearly within grasp. Plainly, there would be great advantages if the same network could provide its users not merely with versions (printed, or electronic) of articles of interest but also with copies of articles cited in the list of references. The utility of such a system will depend critically on the degree to which the literature as a whole accumulates in electronic form. Searches of the electronic literature for relevant contributions not included in the cited references would also be valuable. Electronic versions of the primary journals could be combined in the same network with more advanced versions of the bibliographic files of titles and abstracts that have made a modest contribution to many people's awareness of the scientific literature in the past decade or so. This, however, is yet another benefit that will accrue only when the process of making the literature electronic has absorbed a substantial part of the whole.

The disadvantages of this way of organizing the scientific literature are, unfortunately, less easily identified. Although it is now customary to suppose that computer technology can be adapted to any task whose specification can be defined, experience has shown that computer systems do not always function as smoothly as their designers hope. The development of computer systems which are acceptable to the users of electronic journals, and not just to their designers and editors, will be slow and expensive. The costs of operating and using electronic journals cannot even be guessed at this early stage. The most obvious difficulty is that the initial costs are certain to be very large. Would-be users will have to equip themselves with communications terminals at a cost that far exceeds the annual subscription to even the most high-priced journals.

Even less tangible disadvantages may be more serious impediments to these developments. Even within the scientific community, people are conservative in their habits. Browsing through the scientific literature, not necessarily in a single narrow field, is not merely pleasurable but educative and stimulating. Will the communications terminals of the future lend themselves to such a practice? But people also appear to like carrying their favourite journals around with them, reading them at home or on some journey. Will a sheaf of hard-copy paper produced by a communications terminal serve the same purpose? People are, in short, attached to the printed word in its familiar form. Those who are now planning electronic journals are no doubt aware of the subtlety of the needs they have to satisfy. Defining them, however, will be a formidable undertaking. Experience may yet show that they cannot be met.

The ecology of mental process: a life of Gregory Bateson

Edmund Leach

Gregory Bateson: The Legacy of a Scientist. By David Lipset. Pp. 360. (Prentice-Hall: 1980.) \$16.95, US only.

IMAGE
UNAVAILABLE
FOR
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REASONS

Gregory Bateson, 1958

MARGARET Mead died in November 1978, Reo Fortune in November 1979, Gregory Bateson in July 1980. The conjunction of these three most unusual anthropologists in New Guinea at the end of 1932 drastically restructured their private lives. Mead, who was then married to Fortune, was later married to Bateson for 14 years. The consequences for scholarship are still difficult to assess. Fortune ceased altogether to be an effective anthropologist; Mead became an international celebrity, mainly by virtue of highly impressionistic, easy to read, accounts of field research which had already been completed when she first met Bateson. Bateson's principal contribution to anthropology, the awkwardly complex but highly original *Naven* (1936), was also based on fieldwork that had been completed by late 1932, and which was written up in Cambridge before his marriage to Mead. But although it is a very different sort of book from anything that

either Mead or Fortune might have written, it would probably never have been written at all without their stimulus.

In 1936 the dominant style in British anthropology was the extreme empirical functionalism adopted by Malinowski and his pupils, Raymond Firth and Audrey Richards. Bateson, while declaring his respect for the work of this school, also argued that the best ethnography has the artistic merits of a great novel. In his opening pages he invoked the names of Jane Austen and Charles Doughty's *Arabia Deserta*.

Naven was an attempt to capture what Bateson called the ethos of Iatmul culture rather than simply to describe, in Malinowskian manner, how everything fitted together. The general attitude to ethnographic evidence which Bateson adopted, which was made to seem quite unnecessarily obscure through his mode of presentation, had much more in common with the later work of Evans-Pritchard and of Lévi-Strauss than it had with then current fashions. But although *Naven* was ridiculed at the time by Malinowski, along with Mead's *Sex and Temperament in Three New Guinea Societies* and Benedict's *Patterns of Culture*, it was a book that was read with great interest by Malinowski's younger pupils, as I can vouch from my experience.

Bateson usually described himself as an anthropologist, but he also had polymathic interests in such fields as animal behaviour, cybernetics and the psychology of schizophrenia. His enduring reputation, which may well prove to be very considerable, is likely to derive as much from these other interstitial activities as from his direct contributions to anthropology.

Lipset's biography, which was published a few weeks before Bateson's death, is a brilliant performance. He had the full collaboration of Bateson himself and of all members of his entourage, including access to family papers and letters, but many of the most interesting passages in the book derive from the personal recollections of those who had known Bateson and whose opinions, as expressed in unstructured interviews, were recorded by Lipset on tape. A great variety of people collaborated in this way, including both Mead and Fortune, and the author has shown astonishing skill and tact in deducing, from what must often have

seemed very contradictory and prejudiced evidence, a balanced account of the life and intellectual development of a man whose persistent curiosity about matters which most of us take for granted sometimes came close to genius.

Bateson's family background was academic Cambridge in high degree. His grandfather, W. H. Bateson, was master of St John's College from 1857 to 1882; his father, William Bateson, was the celebrated zoologist whose renown stemmed from his pugnacious vindication of the genetics of Mendel against the statistical biometrics of Weldon and Pearson. William Bateson invented much of the technical language of modern genetics including the word "genetics" itself. Gregory was clearly greatly influenced by his father; indeed his first publication was a joint-authorship contribution to the *Journal of Genetics* "On certain aberrations of the red-legged partridges . . ." (1926), published when Gregory was 22.



William Bateson, July 1907

But Gregory's intellectual heritage was not restricted to biology. It was William Bateson who first introduced Geoffrey Keynes to the art of William Blake, a field in which Sir Geoffrey, at the age of 93, is

now an acknowledged world authority. This was an enthusiasm which Gregory shared and which is somehow reflected in much of his later work. But probably the most important influences on Bateson's thinking came from his close friend C. H. Waddington, the Edinburgh geneticist. Gregory never adopted the Marxist view of science favoured by Waddington, but he did share many of the latter's humanist concerns. What these concerns were is summed up in the titles of Gregory's last two substantial publications, an essay collection, *Steps to an Ecology of Mind* (1972), and *Mind and Nature: A Necessary Unity* (1979), the latter written at a time when Gregory was fully aware that he was suffering from terminal cancer.

Gregory was not a vitalist; he saw very clearly that the scientific explanation of human behaviour must be of essentially the same kind as the scientific explanation of the behaviour of dolphins. But he was too good a cultural anthropologist to be taken in by the kind of reductionism that is favoured by some of the more simple-minded sociobiologists. The human mind cannot be explained away either as a genetically pre-programmed machine or as an illusory side effect of conditioned reflexes.

Gregory's interests always remained biological; but the focus of his attention was not confined to the human being as a biological organism. It was Man in his social interactions and Man as a species adapted to extremely sophisticated forms of interpersonal communication that provoked his most challenging suggestions. But they were suggestions rather than proven facts. His theories about the nature of schizophrenia and about "the double bind" influenced a wide variety of practising psychotherapists, but they were often misunderstood and they were not of a sort which lend themselves to verification.

Academically he was always a loner; he seldom occupied any position which called for formal teaching. He exercised his influence in private informal seminars and conference discussions and it is difficult to pin down just what that influence was. Gregory was a guru. I know that I myself found him one of the most exciting and inspiring "teachers" I have ever met.

Gregory himself would probably have claimed that his main claim to fame was his application of ideas borrowed from cybernetics to an understanding of the feedback which occurs in person to person interactions. But what he had to say on such matters often contained a good deal of blarney; he had a scientific attitude, but he was not an exact scientist and he was not a mathematician.

Lipset recognizes these limitations. Inspired in his youth by the art of Blake and the laws of Mendel, Gregory aspired to make comparable innovations. He did not succeed, but his contributions to our understanding of the position of mind in

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From left: Gregory Bateson, Margaret Mead, Lois Bateson and Barkev Kasarjian

the physical world and to the complex relationships which link form and process are far from negligible.

There is much more to Lipset's book than I have been able to summarize here. The account of the intellectual atmosphere

in which Gregory grew up is particularly impressive. The book as a whole makes a most timely and fitting memorial. □

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Beveridge on discovery

P. B. Medawar

Seeds of Discovery. By W.I.B. Beveridge. Pp.130. (Heinemann/W.W. Norton: 1980.) Hardback £6.95, \$12.95; paperback £3.90.

THIS book is a sequel to the author's lively and readable *The Art of Scientific Investigation* (Heinemann, 1957). *Seeds* is readable too — not least because of the wealth of anecdotes and other illustrative material which help the author to make his points; it is a learned man who will learn nothing from Beveridge's pages. Amidst much that is familiar I was very interested to learn that a former Vice President of the National Academy of Sciences had published a demonstration that flight by heavier-than-air machines was not possible.

The present book is not nearly such a success, unfortunately; it is not very original and is in places lamentably trite. Nowhere was I struck, as one always hopes to be, by some felicity of thought or writing. Indeed, I found myself in the disagreeable position of having reason constantly to find fault. As to triteness, consider such a passage as this:

Scientists do not work in isolation. All are members of the world-wide scientific community. It is joined together by

communication through scientific journals and meetings, which are an essential part of science. Formal and informal discussions at scientific meetings, sometimes involving conflict of views and arguments, are a feature of the scientific life.

This is the writing of someone who has nothing very original to say.

The book throughout has a slightly aggrieved and truculent air arising mainly out of the very low opinion Beveridge holds of philosophers of science, whom he accuses of trying to foist on us the notion that scientists operate something that might be called 'the scientific method' — the existence of which, as he rightly says, is a myth. Of the leading philosophers of science, however, it was only Francis Bacon and John Stuart Mill who put before the public an integral body of thought — an organon — that could pass as an exposition of 'the scientific method'. Popper did not, nor did Kuhn. Among Beveridge's many causes of complaint is that philosophers of science have "failed to appreciate the cardinal role that chance and opportunism play in research, and most have dismissed the subject as hardly worthy of their serious consideration".

But what form could such a consideration take? If the story of the remarkable conjunction of events that led to the discovery of penicillin were recounted to a philosopher, what could he say except "Why, gee, what amazing strokes of luck!". If Beveridge himself were a little more philosophical about the matter, he would see that there is an inherent bias in our estimate of the contribution of good fortune to scientific research: we can all recognize when good fortune leads to a discovery or enlarges the understanding, but from the very nature of things we cannot know how often bad luck deprives us of the chance of making a discovery we might otherwise have made.

The most interesting paragraphs in Beveridge's book are those in which he deals with various expedients for promoting the flow of original ideas. Not all are convincing: the more I read and reflect upon the virtues of 'lateral thinking', the more I wonder what all the fuss is about. To be sure, we should all try to be adventurous in our thinking and try to get out of familiar ruts; but this is advice such as Polonius might have given — it cannot come to anyone as a revelation.

Beveridge criticizes Popper, as others have, for failing to throw much light on the process of ideation — the process by which new hypotheses come into being. Popper rebuts this charge perfectly adequately by pointing out that his work is mainly upon the *logic* of scientific discovery, and that ideation is outside logic and is a logically unscripted process. However Popper is fully aware of the central importance of having ideas as the generative act in scientific enquiry. In spite of Beveridge's criticisms I believe him to be more indebted to Popper than he realizes. In his final chapter, for example, he is clearly feeling his way towards the concept that Popper embodied in the notion of a 'Third World' (*Popper's Third World*; see *Nature* 241, 293; 1973), though Beveridge clothes it in the tiresome terminology of 'hardware' and 'software' — an inappropriate terminology in this context because many ideas and conceptions are embodied in hardware such as machinery, buildings, institutions and so on.

One of the passages in which Beveridge seems to lack philosophic understanding is that in which he deals with frauds. In recounting the Piltdown hoax, brought up to date by incorporating Stephen Jay Gould's suggestion that the principal conspirator was none other than Teilhard de Chardin, he says that its main interest is to show "that even the scientific Establishment can be fooled by evidence that in retrospect is seen to be an obvious fake"; but does not Beveridge realize that science, like banking and government and — if that wise man Kenneth Clark is to be believed — civilization itself, rests upon confidence. When we go about our business we do not expect our colleagues and coworkers to be liars; nor do we

scrutinize their statements with wary circumspection, in the manner of men on their guard. If we did so there would be no scientific business to transact. In going on to describe Paul Kammerer's fraud, Beveridge says Kammerer's views on the nature of inheritance were quite incompatible with those of neo-Darwinists "who believed that evolution was due solely to the selection of chance mutations that favour survival". This is a travesty of neo-Darwinism, but it would take too long to explain why.

Accounts of the Summerlin scandal and the fraud implicating Sir Cyril Burt pad out the book readably, but their inclusion may give a rather distorted picture of science to the young scientists who are among those to whom the book is addressed. I surmise — for there can be no proving such a statement — that for every scientist who fiddles his results there are a thousand who do not, and for every scientist who waxes fat on the proceeds of deception a thousand others spend sleepless nights and days of sick anxiety for fear that they have been guilty of a factual misrepresentation — or even, what does not matter nearly so much, of propounding an erroneous hypothesis.

"... most eminent scientists I know do have a lively sense of humour" says Beveridge — a characteristic he chooses to

illustrate by referring to Waddington's witless and disagreeable acronym COWDUNG which stands for 'conventional wisdom of the dominant group'.

Beveridge has some wider views on science in education which I find as difficult to accept as many of those that relate to science itself. He writes that "... it would benefit everybody if the education of scientists included more studies in the humanities ...". I wonder: my own view, as ill-founded as his own, is that the young scientist who has not the initiative and the will to read books or listen to music or visit galleries will be bored out of his mind by lectures of the quality he is likely to receive on subjects such as 'the English novel' or 'the origins of the Romantic movement in Germany'. It would be a different story, of course, if an Ernst Gombrich or Kenneth Clark were to be found on every campus; but what *can* be found on every campus are libraries, radio, television, records and enthusiasts eager to share their enthusiasms — all of which may help to enlarge human sensibilities or human understanding. □

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Freudian variations

Stuart Sutherland

Freud: The Man and the Cause. By Ronald W. Clark. Pp.652. (Cape/Weidenfeld & Nicolson/Random House: 1980.) £9.95, \$19.95.

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FREUD was nearly 40 when he began to develop the psychoanalytic ideas for which he is remembered, but even as a youth he was convinced that he would be a famous man. From the age of 21 he periodically tried to destroy all records of his private life in a deliberate attempt to make difficulties for his biographers, each of whom would "be right in his opinion of 'The Development of the Hero'." The latest to take up Freud's challenge is a highly

professional biographer, Ronald Clark, who has already tackled Einstein, J. B. S. Haldane and Bertrand Russell. Fortunately for Clark, Freud's correspondents did not always obey his injunction to destroy his letters and considerable new material has come to light since Ernest Jones wrote the mammoth official biography.

The standard view of Freud's life, as put forward by Jones and other followers, is that he was indeed a hero. They argue that his theories were for long either ignored or derided because of their shocking sexual content, he was denied promotion, he fought with the world in "splendid isolation", and psychoanalysis emerged almost entirely from his own head (or genitals) as a result of his heroic self-analysis. Freud, himself, in his autobiographical writings did everything he could to encourage this view.

In recent years, several scholars have attempted to modify the myth of Freud's heroism. His ideas received considerable support almost from the outset; to the extent to which they were rejected, it was because they were old-fashioned (for example, his attribution of some neuroses to masturbation) or obviously wrong (for example, his belief that many neurotics had been sexually seduced in infancy by an older person). At no time was he isolated from the rest of the scientific community, and many of his ideas were either modifications of existing lines of thought

or were developed in collaboration with others, particularly with Wilhelm Fliess with whom he was in regular correspondence throughout the period when he was developing the basic ideas of psychoanalysis. It is significant that despite their intimacy and the overlap in their work and ideas, Freud does not so much as mention Fliess in his autobiography, and he tried to have his letters to Fliess destroyed. The revisionist view of Freud's career is well summarized by Frank Sulloway in *Freud: Biologist of the Mind* (Deutsch, 1979) which was published too late to be of use to Ronald Clark in writing his own biography.

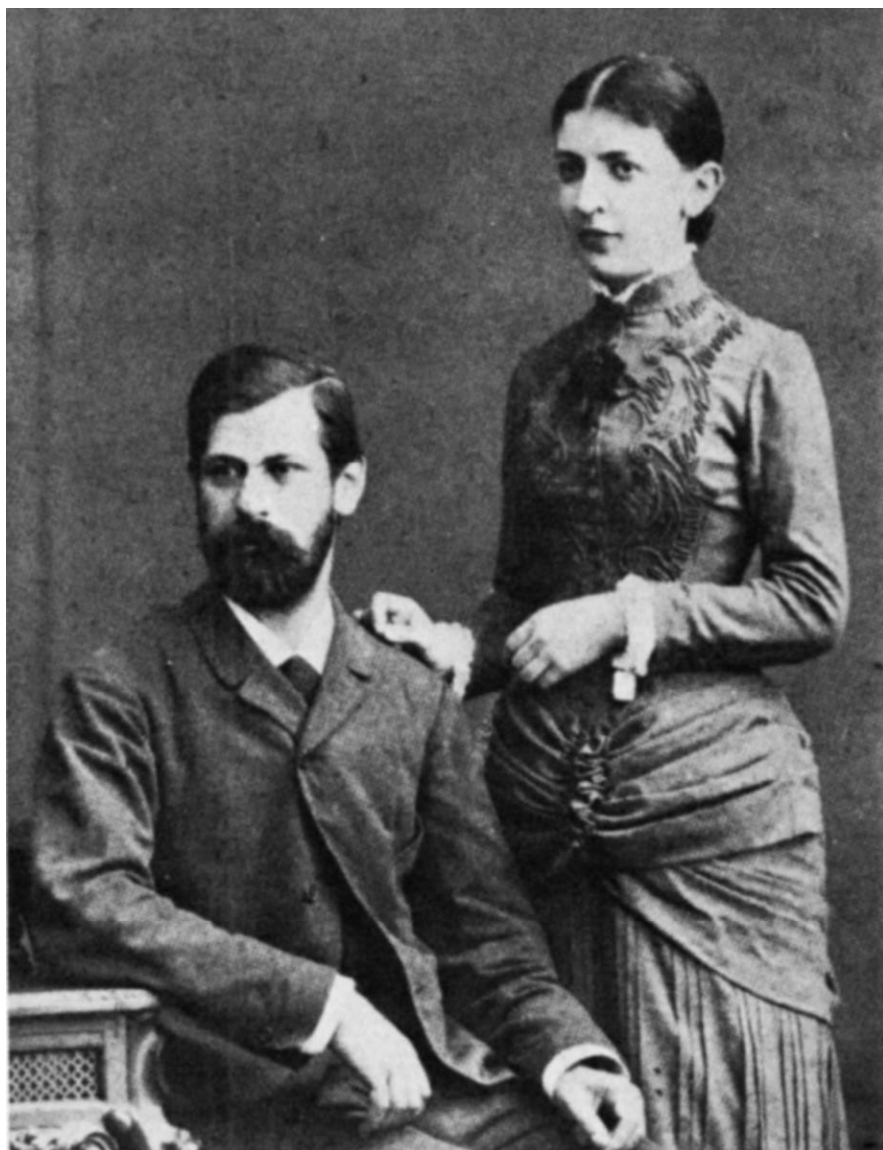
Clark takes a middle-line on these contentious issues. He concentrates on Freud the man rather than on the intellectual content and origins of his work. On Freud's personality there is little new to say. He was often tetchy and intolerant, as when he reproved his wife for talking to strangers in a restaurant. He could be extraordinarily vindictive: although he formed intimate friendships with several men (such as Breuer and Fliess) the friendships did not last and, once they were broken, Freud never forgave. He loudly proclaimed that psychoanalysis was a science, but he treated it as a religion: he was merciless to the many followers who dared to depart from the orthodox doctrine as laid down by himself. On defection, Morton Prince became "an arrogant ass", Magnus Hirschfeld "a flabby, unappealing fellow", and Carl Jung a "megalomaniac" and a "miserable pen-pusher". One wonders how much insight Freud had into his own childishly defensive reactions.

Another of Freud's persistent traits was that he took great delight in annoying others. Of his fiancée's mother, he wrote "I can foresee more than one opportunity of making myself disagreeable to her and I don't intend to avoid them". He stayed away from one neurological congress because "our absence should annoy them and that suits me". It is likely that Freud's failure to achieve rapid academic promotion was caused more by his own prickly personality than by his Jewishness or the unpopularity of his ideas.

His lust for battle and intellectual arrogance polarized opinion on psychoanalysis. He gave those who were not wholly for him no option but to be against. He made matters worse by his reluctance to admit his own mistakes: for example, he did not publicly disavow his infantile seduction theory until many years after he had himself abandoned it.

In contrast to his behaviour with friends, he seems at least in adulthood always to have been generous and kind towards both his immediate family and his more distant relations. But they would appear never to have crossed his wishes and to have treated him as their natural leader.

Perhaps Freud's greatest virtue was courage. In the last 16 years of his life, he had over 30 operations for cancer of the



Freud and Martha Bernays, photographed in Wandsbeck, her home outside Hamburg, in 1885

mouth and had to wear an uncomfortable prosthesis. He bore the pain and danger with the greatest stoicism, continuing both his writing and his clinical work. When it became clear that he was dying, he calmly asked his doctor to put him out of his suffering. In the face of all medical advice, he went on smoking large cigars to the end of his life.

Freud: The Man and The Cause records all this and much more, yet at the end of the book most readers will feel that they have not learned what Freud was really like: his own secrecy about himself and his determination to act the part of hero make it difficult to unravel the inner workings of his mind. Moreover Ronald Clark records events, but passes few judgements of his own.

Perhaps wisely, he neither interprets Freud's life in psychoanalytic terms, nor does he derive Freud's psychoanalytic ideas from his life. The clues to the latter problem are tantalizingly few: Freud had a doting mother; as a young man his attitudes towards the opposite sex were

prudish; his friendships with members of his own sex were highly emotional; and he appears to have given up all sexual activity from the age of 41, by which time he was in the midst of his own self-analysis.

Clark describes the elements of Freud's ideas clearly, but at an elementary level: his excellent index contains no reference to such terms as "displacement", "projection", "regression" or "polymorphous perversity". He makes little attempt to evaluate Freud's work and when he does he is often wildly wrong. For example, he attributes recent revisions of psychoanalytic theory to unspecified advances in biochemistry, and quotes with approval Bertrand Russell's silly criticism of Freud's theory of dreams that "we cannot know what a man dreams, but only what he says he dreams": as far as psychoanalytic theory is concerned, it is irrelevant whether the patient has actually dreamt something or merely thinks he dreamt it.

Clark cannot be altogether blamed for his failure to assess the importance of Freud's ideas. Psychologists still know so



Freud (left) with Wilhelm Fliess, his confidant during the early years of psychoanalysis

little about the forces that motivate human action that the ultimate value of Freudian theory cannot be assessed. It is certain only that much of the theory remains vague and that Freud often overgeneralized: his concentration on the libido and the Oedipus complex as the main influences in the development of personality was mistaken. It is doubtful if present-day psychology would be much different had Freud never lived: his main influence has been on the patterns of thought of the layman and hence on much twentieth-century art and culture. Moreover, there are many who feel that Freud sent psychotherapy in a wrong direction, and that it has only recently

begun to recover from the damage done by his ideas. New therapeutic developments are much closer to Adlerian practice than to Freudian.

There are no pyrotechnics in Ronald Clark's new book, but he has made available in one place a mass of previously published material and has added some facts of his own discovery. Although he has not broken the enigma of Freud's personality, he has produced a highly professional biography. □

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What is it that we know?

D.V. Lindley

The Enterprise of Knowledge: An Essay on Knowledge, Credal Probability, and Chance. By Isaac Levi. Pp.462. (MIT Press: 1980.) \$27.50, £17.

A SUBSTANTIAL part of the knowledge of the world that we have today is the result of the activities of scientists. If knowledge is thought of as a tool by which we may control the world, then scientific thinking is pre-eminent. Artists may help our understanding, but it is scientists who develop the techniques and ideas of control. It is therefore surprising that scientists have paid so little attention to the appreciation of how knowledge is acquired and manipulated. Kuhn has pointed out that most scientific work consists of following through a standard set of techniques, or paradigms, and that the individual is so absorbed in the technicalities of the apparatus, the field, or the mathematics, that he never needs to think about the basis of what he is doing. Other scientists, a small but significant minority, do think more widely but again are

typically not concerned with the nature of knowledge. There are exceptions: for example, Medawar's delightful *The Art of the Soluble* (Methuen, 1967) and, perhaps the most important of all, Harold Jeffreys' *Theory of Probability* (Clarendon, 3rd edn 1961).

There are two groups of people who do think about the knowledge business: statisticians and philosophers of science. The former have developed methods of processing data and reaching conclusions that have gained wide acceptance in some branches of science, so much so that it is scarcely possible to publish a paper without the accepted statistical support. Other scientists pour scorn on statistical methods and regard experiments that require statistical analysis as poor experiments: these are the builders of expensive, laboratory equipment. The philosophers have thought and written a lot about scientific method, and have recently considered the statistical techniques as part of that method.

There is one conclusion that all

statisticians and most philosophers now agree upon: the description of our knowledge, and the way that knowledge is used in control, are essentially probabilistic. There are, however, substantial differences on how probability is to be used and what it means. The accepted paradigm of statistics uses probability only in the sense of frequency, so that we may speak of the probability of the experimental results, which may be repeated, but not of the probability of the hypotheses, which cannot. A minority of statisticians, and perhaps the majority of philosophers, think of probability as a direct descriptor of knowledge, so that probabilities of hypotheses are admitted. Some think of this probability as subjective, some as objective. Here philosophy is providing usable, and — it is to be hoped — useful, results; scientists ought to take note.

In this book, Isaac Levi talks of what he chooses to call credal probability as the way of evaluating hypotheses. Knowledge is thought of, not as a collection of results, but as an input to rational decision-making — "Epistemologists ought to care for the improvement of knowledge rather than its pedigree". The same should be true of scientists. Levi is thus no scholar isolated from practice, but a scholar who is concerned with application as the basis of our thinking. (An appendix discusses the use of his ideas in assessing accident risks in nuclear power plants.)

He therefore disagrees with most statisticians' view of probability as only frequentist — in such situations he talks of "chance" — and devotes a fair portion of the book to a criticism of the methods they have developed, paying special attention to Fisher's concept of fiducial probability, a concept that exerts a fascination out of all proportion to its value. His view is the Bayesian one that probability applies to all uncertainty, not just to repeatable phenomena; so that we can speak of the probability of isolated events, or of hypotheses. What Levi calls a "strict" Bayesian, says this probability is unique and definite, and expresses the totality of our knowledge. In conjunction with utility (which receives little discussion in the book) decisions can be made by maximizing expected utility. Levi does not agree with this uniqueness and admits a set of probabilities. This leads to a difficulty, since the existence of many probabilities leads to many expected utilities, and choice between them has to introduce other considerations. He uses a maximin device in which the worst possible outcome is made as attractive as possible. (It is a pity he does not discuss the objections to maximin that exist, especially as he uses a restricted form of that criterion to which they may not apply.)

Levi writes as a philosopher and the emphasis in his treatment is on the ideas rather than their execution. He discusses at length the related ideas of other

philosophers, especially Kyburg and Hacking who have written on probabilistic ideas and is critical of Popper's appreciation of scientific knowledge. And yet his treatment is often realistic, since it is always set against this decision-making, operational background. Thus he criticizes the adherents of the likelihood view, and Shackle in particular, by saying:

The point is, that calling a mode of appraisal a way of measuring or assessing support is not helpful. A specification of the use or function of the mode of appraisal in inquiry and deliberation is needed, whether the method is probabilistic or not.

This is not an easy book to read. It is very long and parts of it are rather technical. For someone concerned with logical questions, his definitions are not as crisp or as clearly laid out as one might wish. There are many parts where the language is turgid; this is his definition of L-irrelevant:

... the information that a trial is of kind T is L-irrelevant to the issue as to whether an R occurs on that trial relative to information that the trial is of kind S if and only if K contains the information that being of kind T is stochastically irrelevant to yielding an R on a trial of kind S.

A more serious point of style that disturbs me is his failure to help the book's readability by adopting standard notation. For example, experts in the probability calculus use $p(A|B)$ for the probability of A given B. Why then use $Q(h;e)$? And why use irrelevant instead of independent? Much of the later sections of the book are difficult going because of the apparently unnecessary changes of language and notation.

It is a pity that Levi has so little to say

about works of the "strict" Bayesians, de Finetti, Jeffreys, Savage, Ramsey and others. Is he fully aware of the basic result that a man who is to act sensibly can only do so if he acts in accordance with a *unique* probability and a *unique* utility? And why is there no mention of exchangeability, that brilliant notion expounded by de Finetti in his two-volume treatise *Theory of Probability* (Wiley, 1974/5), that connects chance with belief and embraces the frequentist framework within that of knowledge? Levi says in his discussion of nuclear safety, that "the available evidence fails to warrant a sufficiently definite system of credal probability judgments"; but probability is the only description of the available evidence, as Ramsey and others have shown. We may not like the evidence, but probability should not be the scapegoat.

Where does this book stand as a contribution to the study of knowledge? Its importance lies in its new emphasis on a general, credal probability and in its forward-looking, decision-orientated view of knowledge. It leads us further along the road towards a philosophically satisfying, yet usable, appreciation of scientific method: an appreciation that could do much in a really practical way to assist the development of science and technology. And yet, is that not already with us in the work of the "strict" Bayesians? It is to be hoped that scientists will think about these issues, and read de Finetti and Jeffreys as well as Levi. □

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Fit for mankind: a vision of Earth

Paul A. Colinvaux

The Wooing of Earth. By René Dubos. Pp.183. (Athlone/Scribner's: 1980.) £7.50, \$8.95.

To woo the Earth means to coax our countryside into the human image of what the good Earth should be. And the image is often very good; a land fair and open, contrived to reflect an ancient savanna where our species was moulded by evolution, long, long ago. We have done this everywhere and the carpers among us are wrong to call our doings bad. This is the Dubos message of good cheer.

Europe is beautiful, with its vistas of villages, pastures and trees. The European wilderness of the old times, where immense, dark forest forever hid the view, was a frightening place. Greece is delightful, even though its shimmering hillsides are only kept bare by relentless overgrazing. New Englanders like their patterns of village and farm, and their

legislators are trying to stop land going back to forest as farms are abandoned. Lovely parklands like the Han dynasty Summer Palace or the creations of Capability Brown are not wilderness but nature contrived to fit the human appetite. Hardly any of us want wilderness. Why not admit this — and be optimistic about how we can change the Earth without ruining it.

Dubos points out that the sainted Thoreau had a comfortable time at Walden Pond, close to the safety of tranquil Concord, and that the sight of a real wilderness of trees in Maine shocked him to hasty retreat. We pay lip service to the wilderness, but most still turn away from its frightening possibilities. We urge Africans to save the game herds, but the Africans will destroy them before the year 2000 because farm land is better than wilderness supporting wild beasts. This seems so self-evident that I have long marvelled at the hopes of those who thought the Serengeti would be saved. We

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destroyed our wild animals in Europe and North America, and took their land; we even make newspaper headlines of the escape of a lion from the zoo and public peace comes back only when it is known that the animal is shot. Why should we expect poor farmers of Africa to act differently?

Dubos stresses that they will not, that people do not like wilderness, that we may save some areas as places for adventuring or because it seems sense to keep the gene pools of wilderness species as intact as possible, but that we ought to replace most wilderness with something even better.

Dubos is asserting that there is a silent majority of people who want a friendly, humanized Earth to live on — not danger, not wilderness, not even what is productive or the result of good ecological management, but what is familiar or beautiful. Doubtless he is right, and doubtless the silent majority will have its way. I worry, though, at the tyranny of majorities to those few who, people-like, do not always run with the herd. A real wilderness is marvellous in ways that Thoreau could never feel. A desolate mountain top in the Brooks Range is a better place to be than a man-made space above the English Lakes. To stand, thinking yourself into invisibility in the Amazonian forest, alone and as the hours pass, cannot be equalled in a botanic garden or in the landscapes of a potentate. A proper wooing of Earth will see that she keeps bits of her wild temper intact.

Dubos tries to show that what people like is what they were programmed to like in ancient days when our species was fashioned in some forgotten African savanna. These parts of the book make uncomfortable reading. We are the learning species, the animal who learned to live in almost every habitat of the Earth before we discovered, through agriculture, how to transform our habitats. Yet Dubos sees the Peking Summer Palace as an attempt to recreate the supposed savanna of our species' youth. This has a feel of genetic determinism about it which is not quite nice. The essential thesis of wooing the Earth can stand without this.

Nor does the Dubos thesis need bolstering by ecological theory, yet his is a conservation ethic of sorts and all conservation nowadays argues before the "Court of Ecology". Dubos would have done better not to, for his is still the ecology of the environmental movement with the standard errors.

It is not a fact that ecosystem complexity yields stability. This was a hypothesis of the 1960s, built out of inspired speculating by Robert MacArthur (*Ecology* 36, 533–536; 1955) who drew mathematical analogies between junctions in information networks and species in ecosystems. By the mid-1970s, R.M. May (*Stability and Complexity in Model Ecosystems*; Princeton University Press, 1974), D. Goodman (*Q. Rev. Biol.* 50, 237–266; 1975) and others had shown how unrealistic this

was and many of us ecologists felt grave disquiet years before then. Modern conservationists appealing to ecological Courts really must read up the latest Court Decisions before applying their ecological law.

It is dangerous practice to talk about how ecosystems "evolve"; change they do, but to talk of them "evolving" suggests a mechanism of selection, of the stable replacing the unstable, the productive the unproductive. There are indeed ecologists who seek supra-organismal patterns of evolution like these — but they are not all of the profession and they may not be the wave of the future. Far better to remember that most of the energy flux used to drive an ecosystem is degraded in the non-living portions. In temperate forest some 0.7 per cent of incident solar energy enters the biota through photosynthesis and the other 99.3 per cent is degraded by raising temperatures or evaporating water (H. Lieth and R. H. Whittaker. *Primary Productivity of the Biosphere*; Springer-Verlag, 1975).

The biota adapt to this energetic reality much more than they control it. Progress towards a nebulous "climax" is a shuffling in line before the energy soup-kitchen, until everyone has found a place of sorts and there is a quasi peace. Incidentally, this is why our human systems have, in general, worked so well; we have altered the arrangement in the biological energy queue without tampering with the main patterns of energy flux. It is only when we do

something terrible to the landscape, such as promoting soil erosion or building a dam, that major diversions in primary energy flux reflect true system instability.

Dubos has a wise and sane vision — an Earth kept diverse and pleasant for human use, made richer by human invention than wild nature had left it. Leave some wilderness for some of us to spend a few hours in and change the rest, ever so gently, until it is good. Yet he protests how well he understands that all will be vain if our numbers keep on growing and that much will be imperilled if we go to nuclear war. But on the ecological subject of human numbers he has nothing to say. He believes that the remorseless rise of population has something to do with curbs in the death rate made by the medical profession and he savours the hope that our numbers may be levelling off. These are views not tenable in ecological logic. Numbers rise because the human breeding strategy remains that of achieving optimum clutch and the destructions Dubos fears will come about as we seek to find adequate niche-space for the surplus individuals that result (P.A. Colinvaux *Nature* 26, 256–357; 1976. *The Fates of Nations*; Simon and Schuster).

Yet it is good to read honest statements that all things done by mankind to the environment are not bad; indeed that most things done have had satisfactory results.

Paul Colinvaux is a Professor in the Department of Zoology at The Ohio State University.

Survival of the fittest author

Wilma George

A Delicate Arrangement: The Strange Case of Charles Darwin and Alfred Russel Wallace. By Arnold C. Brackman. Pp. 370. (Times Books: 1980.) \$12.50.

THIS is a disappointing book. It promises to uncover a plot but fails to convince and fills up pages with incomplete biography. Many people would agree with the author that Alfred Russel Wallace had less than his fair share of publicity but few would agree with his interpretation that Darwin cheated Wallace and that Lyell and Hooker connived at the plot.

Brackman rests his case on dates: the supposed date that Wallace sent his natural selection paper to Darwin and the supposed date that Darwin received it. Wallace thought he sent it in March 1858 and Darwin thought he received it on 18 June but Wallace's envelope with its postmark has not survived. Brackman claims that because Wallace posted a letter to F. Bates on 9 March which arrived on 3 June he must have posted his article to Darwin on the same date and, therefore, the article must have arrived on 3 June.

This is not evidence. This same "evidence" has been used by H. Lewis McKinney in *Wallace and Natural Selection* (Yale University Press, 1972) to claim that Wallace cheated (to say he was where he was not).

Brackman claims that Darwin cheated by saying he had received Wallace's article on 18 June (and not 3 June) in order to quarry it for data and ideas before writing to Lyell. The "evidence" is supported by the fact that Darwin did not keep letters during the 1850s — and that Wallace was a member of the lower classes.

Brackman implies that Charles Darwin or his son Francis destroyed letters because Wallace was writing to Darwin about his ideas on species. But Darwin did not keep letters systematically until he became famous. Brackman also implies that Darwin was surreptitiously using Wallace's 1855 paper on species when the 1855 paper was in print!

Brackman's narrative style is "surreptitious", to say the least: "A troubled Darwin opened Wallace's letter". In fact, it is downright dishonest: "For Darwin his success in securing Wallace a

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Wallace, aged 30 . . .

IMAGE
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. . . and at 46.

measure of security for the remainder of his natural life was an act of expiation". It is a dramatic language: "Darwin understandably panicked". And the reader might understandably panic, too: "Both letters exhibit guile, glibness, and guilt mixed with integrity and honor".

Darwin was distressed when Wallace's 1858 article reached him but distress does not prove guilt. There is no evidence that Darwin plundered Wallace's paper for ideas and wrote them into his own manuscript. Darwin had been brooding on his theory for years and had not written his book and I find his outcry about loss of priority entirely natural. Darwin did not seize on Wallace's idea of divergence and make it his own in the supposed two-week interval between receipt and admission of receipt of Wallace's 1858 article. In 1855, Wallace had written in a paper appearing in the *Annals and Magazine of Natural History* (16, 184–196): "But if two or more species have been independently formed

. . . then the series of affinities will be compound and can only be represented by a forked or many branched line". As for the mechanism, Darwin had written to Asa Gray in 1857 (and the letter is not a fake) of: "an unerring power at work in *natural selection* (the title of my book)" and of a principle of divergence "which shows that organic beings seem to branch out into all the places available".

I find no case against Darwin. I think that the explanation for Wallace's partial eclipse from the evolution-by-natural-selection debate is less dramatic. Darwin's fame came not from the appreciation of a new biological theory by a few members of the Linnean Society but from the intelligent reading public. Evolution by natural selection was a revolutionary theory but the public of Victorian England did not read the proceedings of the Linnean Society. It read books. And the readers, shattered by the convincing mechanism for a process which was already a subject of conversation, were troubled by the implications of the theory for the status of man.

Wallace did not write an *Origin* (it was Darwin who provided a detailed account of the process of organic evolution which was accessible to the reading public) and Wallace developed unacceptable ideas about the evolution of man. Finally, Wallace, the younger man by 14 years, insisted that their theory should be called Darwinism, summing up the situation himself when he wrote to Darwin in 1864:

Animal arms races

John R. Krebs

Tooth and Claw: Defensive Strategies in the Animal World. By J. L. Cloudsley-Thompson. Pp.252. (Dent/Biblio: 1980.) £9.95, \$22.50.

THIS is a popular book about the ways in which animals defend themselves against predators and the counter-adaptions of predators to overcome their prey. It covers similar ground to *Defence in Animals* by M. Edmunds (Longmans, 1974) and *The Ethology of Predation* by E. Curio (Springer-Verlag, 1976), but is aimed at a more general audience.

Most of the text consists of examples, many based on the author's own observations of different kinds of anti-predator adaptation and tricks used by predators to catch their prey. Examples of camouflage, mimicry, venoms, defensive spines, armour and so on are described in a charming and entertaining way. Most readers are certain to come away with at least one or two good coffee-time stories. My favourite is about the African water mongoose, which is alleged to catch birds by sticking its rear end in the air and distending its anus to make it look like a

You had worked it out in details I had never thought of, years before I had a ray of light on the subject, and my paper would never have convinced anybody or been noticed as more than an ingenious speculation, whereas your book has revolutionised the study of natural history.

But I am glad to see a book that publicizes Wallace's contribution to the theory of evolution by natural selection, a book that reprints both the 1855 and 1858 species papers — though it is a pity that Darwin's 1858 contributions were not included for the reader to make his own judgement — and a book that has some hilariously scabrous comments in the "Author's Notes". Wallace's name is heard today much more often than it was in the nineteenth century, partly because of the lessened obsession with the evolution of man and the increased interest in other implications of the theory, partly owing to the work of the historians of science and partly because of the return to fashion of evolutionary zoogeography founded by Wallace and stamped indelibly with his "line". But the more Wallace is linked with Darwin as a co-founder of the theory of evolution by natural selection, the more will historical accuracy be served. Thus, even a negative book like this contributes to the subject. □

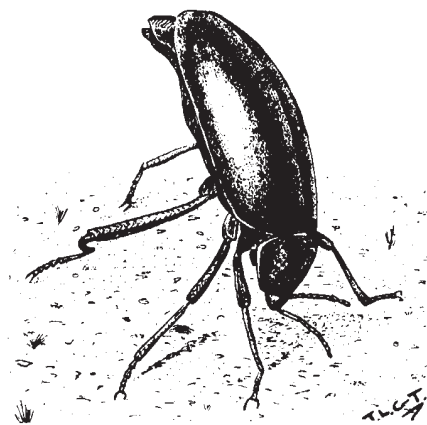
Wilma George is a Lecturer in Zoology at the University of Oxford, and the author of Biologist Philosopher: a Study of the Life and Writings of Alfred Russel Wallace (Abelard-Schuman, 1964).

ripe fruit. Along comes an unsuspecting bird to peck at the fruit and with a smart about turn the wily mongoose snaps it up! Second place goes to the story about frogs' legs and the genitalia of French soldiers in nineteenth century Algeria (without giving too much away, the British are right to stick to pie and chips), and a close third is the account of how large tropical scolopendromorph and scutigermorph centipedes escape from attackers. When attacked or frightened, they shed one of their back legs; the automatized leg leaps around making loud creaking or stridulating sounds to attract the attention of the predator while the nonagintanovipede slips silently away.

Cloudsley-Thompson also tries to extract some general principles about coevolution of predators and prey. He draws a parallel between military arms races and the coevolutionary race between predators and prey. In both military and coevolutionary races, adaptations or innovations by one party call forth counter-adaptations by the other. These counter-adaptations lead in turn to counter-counter-adaptations and so on. One general principle applicable to both kinds of race is the concept of a "trade off" between competing demands. Heavy armour may render a tank less vulnerable

to shell fire, but at the same time it reduces speed and mobility. In the same way animal defences may work well against one kind of attacker but be much less effective against others. The king cobra, for example, is venomous enough to kill an elephant, but is itself killed on occasions by the mongoose with its superior agility.

A closely related idea is that every defensive adaptation has a "cost" which might, for example, be measured in terms of energy that could otherwise be channelled into reproduction. One of the most convincing pieces of evidence for the cost of anti-predator adaptations comes



Chemical defence: when disturbed, *Eleodes* sprays a secretion at the attacker from its abdomen.

from the study of chemical defences in plants (and is therefore not discussed by Cloudsley-Thompson). R. G. Cates (*Ecology* 56, 391-400; 1975) has shown that wild ginger plants (*Asarum caudatum*) in places where slugs are common channel more energy into chemical defence (they taste nastier) at the expense of seed production and growth than do plants of the same species where there is little grazing pressure.

The book touches on some issues without trying to discuss them in their full complexity. For example, in the discussion of Müllerian mimicry (mimicry in which several unpalatable species share the same colour patterns) Cloudsley-Thompson presents the conventional argument that a shared colour pattern reduces the chances that an individual will be killed by a predator in the process of learning to associate colour with distastefulness; the larger the pool of similarly coloured prey

individuals, the smaller the chance that any one of them will be killed. While this argument seems to be correct, it leads one to expect that all unpalatable species living in the same habitat should share the same warning colour patterns. In fact it is known that neotropical butterflies, for example, form several different Müllerian mimicry complexes within the same habitat (C. Papageorgis *Am. Sci.* 73, 522-53; 1975).

The mechanism of evolution of warning coloration is also glossed over, with no mention of R. A. Fisher's suggestion that it might have arisen through kin selection.

However it would be churlish to criticize a popular book for not exploring recondite details. The main aim of Cloudsley-Thompson's book is to entertain and stimulate the reader. In this it succeeds. □

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Animals for the coffee table and student

Bryan Turner

The Complete Encyclopedia of the Animal World. Edited by David M. Burn. Pp. 400. (Octopus: 1980.) £12.95, \$17.98.

THE diversity of animals, the sheer numbers of species, and the richness of their differing forms and functions has always fascinated people. It attracts the curious layman and for biologists begs answers to questions of "how?" and "why?". Although this book has been written and designed to adorn the coffee tables of the general public, students of zoology will find much to interest them. The book is of a higher intellectual standard than that customarily associated with this sort of glossy volume, in part due to the impressive list of contributors. Each section has been written by an acknowledged expert in that particular field. Skilful editing has successfully combined the many and varied styles of the contributors in a way that makes section to section differences unobtrusive.

The text is complemented by a beautiful series of colour photographs and novel illustrations. Although most of the illustrations are useful, some are confusing: for instance, in a figure of the distribution of the geological plates of the Earth's crust the key is absent so that the variously coloured boundaries are meaningless. Perhaps somewhat more important than minor irritants of this nature is the discussion on the links between the chordates and the non-chordates (essentially but not precisely equivalent to the vertebrates and invertebrates). Here the widely held ideas of a link involving the hemichordate acorn worms are dismissed and a new but little accepted theory involving the fossil calcichordates is

expounded. In a general text such as this the most widely accepted views of the experts should surely take precedence, and any new and highly controversial ideas take second place.

The main part of the book is a catalogue of the different groups of animals which is sandwiched between chapters on special aspects of animal life. There are introductory chapters on ecology, in which the biologists' "how?" and "why?" questions are briefly considered, and on taxonomy explaining the classificatory process. This latter section is introduced by a full colour photograph of the book's editor in the guise of a lepidopteran taxonomist supposedly illustrating the qualities of "Patience, experience and a good eye" — perhaps a book on brass instruments will be next! Other specialist chapters include such topics as locomotion, migration, senses, associations, endangered species and a useful section on the major zoos and national parks of the world. The foreword, curiously by David Bellamy, the "Botanic Man", is accompanied by a picture of him riding a tortoise. To ensure that we recognize him, the usually sufficient facial characteristics have been supplemented by those other well-aided taxonomic features — the hairy legs!

These asides apart, this book does represent a good, balanced and informative account of the immense variety of animal life. Although unable in 400 pages to live up to its title "Complete", it is none the less a very creditable contribution from the Octopus stables. □

Bryan Turner is a Lecturer in Zoology at King's College, London.



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The blooming of a hobby: a history of natural history

Alwyne Wheeler

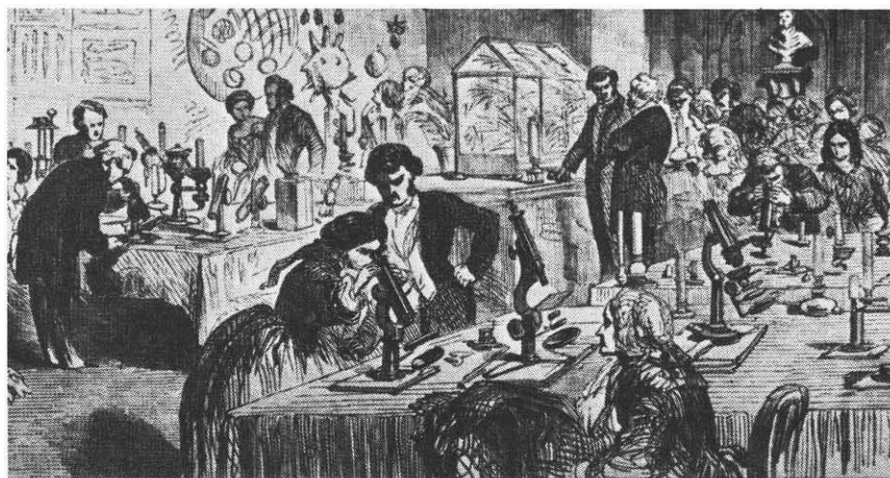
The Heyday of Natural History. By Lynn Barber. Pp.320. (Cape/Doubleday: 1980.) £9.50, \$17.95.

THE middle years of the nineteenth century saw a striking flowering of popular interest in natural history in Britain. The economic and social conditions of the time had produced an increase in the number of literate people who had more leisure and were thus able to utilize their time in what was clearly a health-giving, mind-improving hobby — both worthy objectives in the moral climate of the period. In addition, developments in printing, for example stereotyping and electrotyping, permitted a great increase in the number of popular books, often illustrated with colour plates at relatively low prices.

The result was an extraordinary burgeoning of the literature of natural history written for a popular market. The availability of such books stimulated the interest of even more middle-class naturalists, to result in a cycle of demand and supply which saw the nineteenth century out. The consequences of this great increase in popular natural history and its literature have had considerable influence in our time, for it was during the mid-nineteenth century that many local natural history societies were founded (and those that came later were started by people raised during the period). Many such societies started local natural history museums, and even now have their own publications and libraries, and thus still exert a considerable influence on natural history in Britain although, responding to pressures on the environment today, much of the amateur naturalist's efforts go in supporting conservation-orientated societies.

In this view I differ from the conclusion of Lynn Barber that from the 1870s, in the aftermath of the revolution in thought following the acceptance of Darwin's theories, natural history became "dull". The later years of the nineteenth century simply saw a dichotomy between amateur naturalists and professionals, the latter having been few in number before the 1870s. The amateur interest in natural history has continued as strongly as ever, but the professional naturalists have become more specialized in their fields and in their writings, and few have possessed the breadth of knowledge, the ability or the bravery to produce popular writing comparable to that which flourished in the Victorian period.

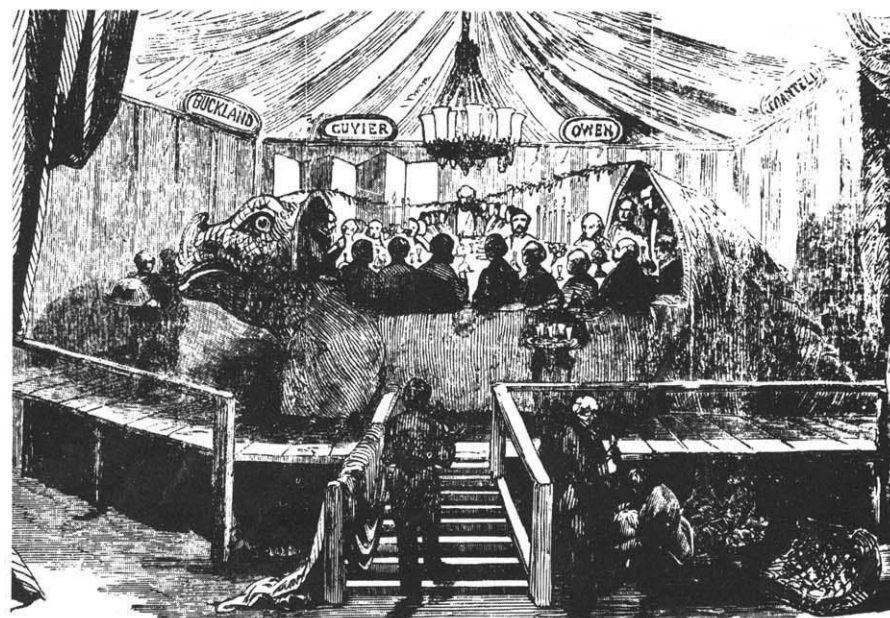
Lynn Barber's book is a most readable account of the great years of the Victorian naturalists (Victorian being loosely applied). The story is a good one, some



"Scientific Conversazione at Apothecaries' Hall", from the *Illustrated London News*, 1855



"Holiday Time at the Zoo", 1872



The Iguanodon dinner, 1854



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superbly interesting characters appear and the material is handled in a masterly fashion.

The first section recounts the social and historical backgrounds, the second contains accounts of Linnaeus, Cuvier, Audubon, Rafinesque, Swainson and Charles Kingsley. Later sections feature Waterton, Gosse, Ward, Mary Anning, the Bucklands, Owen, Sedgewick, Murchison, Huxley and Darwin. But the treatment is not merely biographical; rather, the work and the influence of these "giants" of the nineteenth century is skillfully woven into an account of the development of British natural history, although biographical details have been included to set them in their background. In working this complicated tapestry into an attractively presented, enjoyable and well-written story Lynn Barber deserves all credit.

No doubt it is because of her background as an experienced journalist and broadcaster that her book is presented with such panache. This background may, however, have led her to include some "human interest" stories which are generally now discredited amongst historians of natural history. Thus, the loss of labels from Cuming's mollusc shell collection due to Mrs Gray's carelessness is now dismissed as a canard. Nor was the unfortunate A.W.E. O'Shaughnessy's appointment in the British Museum to work on insects due solely to the influence of his patron as is inferred here; he was simply transferred from one department within the Museum to another, having passed a test of his knowledge of zoology which the other contender had failed.

One has to say that most of the sources used by Miss Barber are secondary. I doubt whether one can rely overmuch on Kingsley's view of Victorian natural history, or on William Swainson and especially not on Audubon for objective



Frank Buckland, naturalist extraordinary

views of their contemporaries. They were all too involved in the period themselves, and Swainson and Audubon certainly had axes of various kinds to grind. The reliance on secondary sources tends to affect the overall images in the book, and also possibly accounts for some of the more alarming generalizations and particular errors. Surely it is not true that between Cuvier's *Le Règne Animal* of 1817 and Darwin's *Origin of Species* in 1859 "almost no major breakthroughs were made"? Two discoveries alone, that of Schwann (1839) of animal cells, and that of the mammalian ovum by von Baer (1827), would today be given the accolade of "breakthroughs".

For these and other reasons Lynn Barber's book cannot be credited as an original history of natural history, but as a readable and well-produced introduction to the subject it is unsurpassed. □

Alwyne Wheeler is editor of the Archives of Natural History (formerly the Journal of the Society for the Bibliography of Natural History) and works at the British Museum (Natural History).

The "why" of animal culture

W.C. McGrew

The Evolution of Culture in Animals. By John Tyler Bonner. Pp.216. (Princeton University Press: 1980.) £8.10, \$14.50.

A DISTINGUISHED cell biologist, J.T. Bonner, has written an ambitious book on the behaviour of animals. In it, he tackles the question of culture as a direct product of the evolutionary processes of natural selection: "[Culture] . . . is as biological as any other function of the organism, for instance, respiration or locomotion". In addressing social scientists, Bonner does not shrink from the implications of this position for human culture and confronts the issues in his opening chapter. From the beginning it is a pleasure to find a book so lucidly written and so free of jargon.

The author's ultimate goal is to explain why we (humans) have culture at all. To

appreciate its adaptive significance requires a step-wise reconstruction of its phylogeny, and it is to this task that much of the book is directed. Bonner starts at the most basic levels of evolutionary mechanisms and advances on a broad front. His definitions are as comprehensive as possible; culture is defined as ". . . the transfer of information by behavioural means, most particularly by the process of teaching and learning". (Such a definition is not without faults, for instance it gives no inkling of the cumulative nature of the phenomenon). The author compares the genome and the brain as information-processing structures, with genes and "memes", respectively, as the units of information transmission — here, and elsewhere in the book, he calls upon Dawkins's *The Selfish Gene*. The latter

system is speedier and more flexible, but it is ultimately limited by the former. The emergence of large brains in human evolution is credited to neoteny, that is, the retention of juvenile traits whereby the brain goes on growing in size after the growth of the rest of the body has slowed or ceased.

Having laid the structural groundwork, Bonner turns to the most basic behaviours. A long chapter on animal societies (which draws heavily on Wilson's *Sociobiology*) relies on the premise that culture requires communication, which is most developed in social organisms. Here, and throughout the book, Bonner chooses to start with microorganisms and work his way through progressively more complex multicellular forms. An excellent discussion of genetic flexibility is followed by the introduction of the concept of a dichotomy of behavioural flexibility: single-response behaviour versus multiple-choice behaviour; this appears to be "nature versus nurture" re-labelled.

The real problems begin to arise with the author's treatment of learning and teaching. All social learning seems to be classified as imitation, with no distinction being made between types requiring differing degrees of mental ability — mynah birds and human infants may both learn English, but the learning of the bird is merely mindless mimicry. No mention is made of "mixed" forms, for example observational learning by a combination of stimulus enhancement (social) and trial-and-error learning (non-social). Finally, there is no reference to behaviours which involve communication but not (necessarily) learning, social facilitation of pecking in domestic chicks, for example. Crucial to the author's argument is teaching, which he defines as "... the release of sets of signals specifically designed to alter the behaviour of another individual". This presents a rare example of ambiguity: in a general sense such a definition applies to all communication; in a more specific sense, it leaves open the question of whether or not intentionality (or goal-directedness) is involved. The reader is told that a large share of teaching

by higher vertebrates can be considered as parental guidance, and that a parent will shape its offspring's imitative performance with nudges, pokes and slaps. But, apart from a single anecdote, no evidence of this sort of behaviour is presented. Contrary to the author's conclusion, it seems likely that it is just this sort of teaching which is conspicuously absent in non-human animals.

The book builds toward a synthetic final chapter which I found somewhat bewildering. Norton-Griffiths's exemplary work on the intergenerational transmission of feeding techniques in oyster-catchers is given suitable credit, but a number of other, equally significant studies are not mentioned. The "natural experimental" research into cultural innovation and diffusion in Japanese monkeys rates only one paragraph; an admittedly fascinating anecdote of one-trial, avoidance learning by elephants is given preference to the many studies of culture in non-human primates — Menzel's volume on the subject is ignored; fidelity to nesting sites in migratory birds is emphasized, in spite of the fact that no social learning need be posited, just as it is not invoked to explain the homing of Pacific salmon to spawn; even the memorable example of milk-bottle opening by tits merits only three sentences. Finally, the section on human culture cites no specific examples, and some of its general conclusions will cause disquiet amongst the social scientist for whom the book is intended; for example, the author's linking of the rise of culture to the rise of writing seemingly bars extant pre-literate societies from consideration.

Yet, overall, in this book Bonner has produced a clear, compelling and wide-ranging account of the bases for social communication in animals. However, those more interested in the evolutionary mechanisms of transition from non-human to human culture are left wanting. That particular book remains to be written. □

W. C. McGrew is a Lecturer in Psychology at the University of Stirling and a Visiting Faculty Member at the University of North Carolina at Charlotte.

Rural nostalgia

Kenneth Mellanby

Hampshire Days. By W.H. Hudson. Pp.250. (Oxford University Press: 1980.) £1.95.

COUNTRY lovers will be grateful to Oxford University Press for reissuing this book in such an attractive paperback edition some 80 years after its first publication. W.H. Hudson was a naturalist who observed the countryside and its wildlife wherever he was, in South America or rural England.

His publishers describe him as "a passionate observer of nature", and this is what emerges from his prose. He gives us accurate and perceptive accounts of the plants, insects, mammals and particularly the birds seen in his garden and in the Hampshire countryside. Some scientists may find his description of his feelings, and his attribution of human emotions to birds and even insects, alien to their tastes, but they will soon be brought back to earth by his unsentimental and accurate accounts of life and death in the countryside.

Hudson's love of rural life was mirrored by his hatred for urban living. He disliked

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the townsmen, with "their pale civilized faces — they are out of my world — the real world". His passion was for "wildness — the rude heath, the beautiful desolation; furze and ling and bramble and bracken to grow on me, and only wild creatures for visitors and company". He was of course aware that he was observing not the natural face of England, but the result of the interplay of human activities and ecological processes. He describes prehistoric barrows as well as traditional farmhouse and agricultural activities. But at the time he was writing it was possible to imagine that there was a harmony between man and nature which resulted in the beautiful landscape he so vividly describes.

How he would have hated the changes which have taken place in his beloved Hampshire in recent years. Many of the woods and heaths have gone, some of the hedges have been ripped out. Men are even prospecting for oil! Modern farming is very different from that of his day. Yet a great deal remains. We can, if we are lucky, still see most of the sights he so graphically describes. But few of us have his "seeing eye", and in a lifetime of study may not make all the observations his skill and his sympathy made possible in a few brief years at the beginning of this century. □

Kenneth Mellanby is an editor of Collins' New Naturalist series, which is concerned with wildlife in Britain. His Farming and Wildlife, in this series, will appear in 1981.

Retrospective environmental impact assessment

Eric Ashby

The Volta River Project. By David Hart. Pp.131. (Edinburgh/Columbia University Press: 1980.) £7.50, \$20.

MEMBER states of the European Community will shortly be asked to adopt a common policy for environmental impact assessment. The individual members already have policies of their own; so the wrangling — and there will be plenty of it — will be about the means for predicting environmental impact rather than whether to do it at all. The ends are clear: to reconcile the inevitable conflict between exploitation of nature for the benefit of Man, and conservation of nature also for the benefit of Man. The wrangling begins when you ask: for whose benefit and at whose cost? And the conflict is confused because we do not know how to predict and we cannot agree about who should participate in assessing predictions.

In Britain the current procedure is to hold ministerial enquiries, commonly under the Town and Country Planning Acts. No one pretends that they are satisfactory (think of the bitterness left after the enquiries at Windscale about fuel reprocessing and at Winchester about the route for a motorway); but even critics of the British procedure prefer it to the bureaucratic hypertrophy of the Environmental Protection Agency in the United States. The trouble is that no one seems to be thinking about the problem in a scholarly way, that is, by examining past experience and trying to draw lessons from it. What we need, before we commit ourselves to European policies for environmental impact assessment, are *retrospective* studies of technology assessment and environmental impact predictions. Academics have done a little work, notably Roy Gregory in his book *The Price of Amenity* (Macmillan, 1971), and a team sponsored by the American Academy of Arts and Sciences in their study *Boundaries of Analysis* (Ballinger, 1976). But much more work needs to be done. That is why this modest study of the Volta River project in Ghana deserves careful reading. We may think we manage environmental affairs better in Westminster than they are managed in Accra, but Ghana has something to teach us, even though it is a cautionary tale.

Among people unfamiliar with West Africa there is still a residual euphoria about the great Volta River project. Isn't it exactly what Third World nations need: to enrich themselves by generating energy, creating industries, raising living standards? The message in David Hart's book is that the Volta River project was not what Ghana needed — at any rate not what the great majority of the people of Ghana needed or ever asked for. It was wished on

Ghana by the West: Britain wanted an assured supply of aluminium from the sterling area; the Kaiser Corporation wanted a large supply of electricity with which to produce cheap aluminium. So under the pure white banner of 'aid' the West descended on Ghana, created a lake which occupies 3.6% of its land-area and dispossessed some 1% of its population. (A rough analogue for England would be to flood the whole of Devonshire and to decant its 460,000 inhabitants into other parts of the country.)

The Volta River project was contemplated as long ago as 1915 by the man who was at that time director of the Gold Coast Geological Survey. The idea was revived about 1948. A special commissioner, Commander Jackson, was appointed in 1953 to report on the whole project and its implications, without prior approval from the legislative assembly in Accra (a sign, as Hart says, "that the real decisions were being made elsewhere"). Even at that stage two influential and distinguished members of the assembly, Danquah and Busia, voiced their doubts. The primary purpose of the Volta River project, they said, was the production of cheap electricity to smelt aluminium; the development of Ghana was only a secondary purpose; the people of Ghana would benefit more from a smaller project to supply electricity to many towns, and to provide irrigation.

And so it has proved to be: aluminium is being smelted, but it has not brought the benefits to Ghana that were promised, and its destiny is in the hands, not of the Ghana government, but of the International Primary Aluminium Institute. As to the benefits to Ghana, Hart's account of the plans which were made to re-settle the 80,000 people occupying 739 villages in the

area to be flooded is a sardonic comment on the incompetence of planners when they have to deal with the human consequences of their decisions. Of course there were plans to compensate the people ejected from their holdings and to give them land elsewhere. In the event the plans were so mismanaged that much of the compensation is not paid, even today, and much of the re-settlement has proved abortive. Polygamous extended families, accustomed to having separate houses, however simple, for their wives and relatives, were given a house suitable only for a nuclear family. In their new locations the pattern of their society, the markets — the familiar locations for buying, selling and making social contracts — vanished; even the styles of agriculture and fishing had to be different. From a world of poverty ameliorated by security they were shovelled into a world of poverty exacerbated by stress. There were tensions among the indigenous occupants of the lands where the re-settlements took place. There were scandalous under-valuations of the property some of them had been obliged to abandon. And, on top of all this, there were alarming increases in the incidence of bilharzia, owing to the opportunities for the snail which transmits the disease to breed in the still waters of the lake; Hart publishes a map of the lake showing places where 70–100% of people sampled were infected.

I said that the experience in Ghana may have lessons for Britain; a remark which will provoke the protest: "It couldn't happen here". Not in the same way, it couldn't. But when we plan airports, motorways, power stations, what proportion of cash, thought and effort is put into the second-order effects of the pro-

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The Volta dam — what benefits has it brought to Ghana?

jects? And are the decisions as to what is 'good' for the local populace made locally, or in London? (One perceptive comment on the environmental impact assessment made for the Volta project was that it was made by Westerners for Westerners; what was needed was a team of 'barefoot anthropologists' to live among the people affected by the Volta dam, and then to recommend how they should be handled.) If the people who say "it couldn't happen here" will pause a moment, they may recall the preposterous tragedy of taking people out of down-at-heel terrace houses and hoisting them up into high rise flats; or resettling people from the cohesive and compassionate society of a slum into neat, clean, aseptic villas in a suburb.

Upheavals in our traditional ways of life are inevitable; we are in for a lot more of them; people will have to migrate from the closed steelmills of Corby as surely as they

had to migrate from the waters of the Volta River. The British people are flexible and courageous enough to tolerate these upheavals. What they will not — and should not — tolerate is the pained surprise of planners when some of the remedies proposed from Whitehall are rejected. The way to minimize mistakes — they can't be avoided altogether — is to improve the standard of environmental impact assessment; and the way to do that is to study very carefully case-histories of past assessments, to diagnose where they went wrong and what they left out. David Hart's little book, despite its high price, ought to be on the bookshelves of planners; for he does what he sets out to do: he gives a case-study of politics and technology relevant not only to Ghana but to Britain. □

Lord Ashby is Chancellor of Queen's University, Belfast, and a Fellow of Clare College, Cambridge.

Questions of energy

Joseph S. Nye

World Energy Issues and Policies. Edited by Robert Mabro. Pp.367. (Oxford University Press: 1980.) £15, \$44.50.

THIS volume is a collection of papers from the first Oxford Energy Conference, held at St Catherine's College in September 1979, and cosponsored by the Organization of Petroleum Exporting Countries and the Organization of Arab Petroleum Exporting Countries. The Secretaries-General of the two organizations provide two of the 28 papers in the book. Distinguished OPEC contributors also include Kuwait's Minister of Oil and Venezuela's Minister of Energy and Mines. Other essays are contributed by government, industry and academic figures from various oil-consuming and -producing nations. A brief introduction and summary is provided by the editor, Robert Mabro.

As might be expected in a diverse collection of conference papers, there is great unevenness of quality and style. Mabro explains that the essays have "not been heavily edited" in order to avoid lag in publication and to preserve their flavour of authoritative statements. Fair enough, though the disparities on occasion jar somewhat — a brief section, "World Energy Outlook", pairs Wolf Hafele's 23 pages on world regional energy modelling over 50 years with three pages of casual observations by the late C.C. Pocock of Shell Oil.

A more important problem is the gaps in coverage. The resulting tone of the book certainly leans toward the energy establishment. The editor acknowledges some omissions and wishes he had an environmentally orientated paper to balance the

chapter on nuclear energy written by an industry representative. He also regrets the absence of a contribution from a senior official of a major OECD country such as the United States, but explains that official speakers at the seminar were encouraged to speak off the record. A rule that may have been good for the conference, however, is not good for a book. The result is a meagre two chapters, one on the United States by an academic and one on the United Kingdom by a deputy undersecretary of energy, in the section on energy issues and policies of OECD countries. In contrast, there are six papers (including by highly placed OPEC officials) in the section on energy issues and policies of oil-exporting countries. Moreover, the paper on United States' policy entitled "A Critical Overview", hardly purports to be a balanced presentation.

Despite the problems of unevenness and gaps, there are several useful papers in the volume, especially in the opening section on energy supply. Particularly interesting is the paired treatment of natural gas by Nordine Ait-Laoussine of Algeria and James Jensen of the United States. On the other hand, one would have thought coal deserved more than five brief pages. There are descriptive discussions of the Soviet Union and China by Michael Kaser and John Foster, and many of the papers by officials are of interest not because of their analytical insights, but because of their author's positions. If treated as a smorgasbord, the book succeeds in one of the editor's purposes in that it does present some interesting conference fare for a wider audience to sample.

Mabro also has an explicit political objective: "to improve the chances of

success of any future formal dialogue which Governments sooner or later will have to initiate". In his summary, Mabro says that "the urgent need for dialogue was almost unanimously recognized", but there was little agreement on modalities or scope of the agenda.

The idea of a dialogue between OPEC and consumers is currently fashionable in the aftermath of the Brandt Commission Report. A consumer-producer dialogue might help nations shift their focus to the potential long-term joint benefits to be gained. Such a dialogue might seek inter-governmental agreements to stabilize the oil market; for example, OPEC and IEA countries might agree on production targets and consumption limits (at first separately, and then in joint bargaining) which would allow for modest real price rises over the next decade. A band of prices might be established for the duration of the agreement. OPEC countries would agree to maintain sufficient spare capacity to increase production if a shortfall of production from any subgroup of producers threatened to push prices outside the band. They would cut production (or agree to permit consumers to increase demand above the agreed limits) if prices threatened to fall through the bottom of the band. Additional inducements might be needed to assure adequate production levels. For example, consumers might offer indexing of assets and assurances of assistance and market access for the new OPEC industries. Special credit or aid provisions might be agreed for oil-importing developing countries; some such countries could be included in bargaining sessions.

But a number of hard questions must be answered. Could the agenda be focused on energy? If other developing countries participate, will the world replay sterile North-South debates, but with much higher stakes than in the United Nations? Can the "Pandora's Box Effect" be controlled if nations start down the path to serious international collective bargaining?

Is a reasonable bargain likely? At modest prices there are divergent interests between those OPEC surplus producers who lean toward conservation and the high-absorbers interested in maximizing revenues. Large price increases (which maximize revenues and allow painless production cutbacks) tend to reconcile that division. Would OPEC countries be able to agree to a bargain that meant higher production and lower prices than the market would otherwise determine?

Does OPEC have sufficient cohesion to make a bargain stick? Thus far, OPEC countries have been unwilling to limit their separate sovereign control over production decisions concerning the resource that is their major source of power. They compete for power within the oil arena and they reserve the right to use oil as a weapon in wider political games. Given the politics of oil, and the domestic instability of many

OPEC governments, how credible is an OPEC promise to increase production if a shortfall has political ramifications? And if an unintended interruption occurs, how likely is it that OPEC will be able to restrain the high-absorber members from charging what the market will bear? If, as is probable, they cannot, consumers will have paid higher-than-market prices in normal times in return for broken promises.

Would the benefits exceed the costs? Basically, consumers would gain a formal framework for debating production (and price) decisions that are now entirely in OPEC hands. Bilateral diplomacy can have some of the same effect. How much is it worth paying for this framework?

These questions do not mean that conversations with producer states are not useful, or that restoration of an international oil regime is not a worthy long-term goal. Various bilateral and multilateral discussions are essential. But efforts to reconstruct a satisfactory regime are unlikely to be fruitful unless hard questions have been carefully thought through. The volume at hand provides raw material for such thinking, but poses few of those questions and gives disappointingly few of the answers. □

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The state of Arab science

Ziauddin Sardar

Science and Science Policy in the Arab World. By A. B. Zahlan. Pp.205. (Croom Helm: 1980.) £13.95.

THE past decade has seen scientific and technological activity in the Middle East really come alive. While much of this activity is little more than simple transfer of equipment, expertise and personnel, there are, nevertheless, a number of projects which aim to make a real contribution to science development in the area and provide it with an indigenous base; to this end a number of technological universities and specialized institutes have been established to meet some of the more demanding needs of manpower and research.

The scale of this transfer of technology and its associated problems are in many respects unique and unparalleled, and demand urgent and detailed scholarly attention. Thus one turns to Antoine Zahlan's book with the hope of seeing these developments charted, analysed and placed in an appropriate scientific, social and political context. Indeed, few would be better qualified for such a job.

With so much to relate and analyse, it is sad to report that Zahlan has missed an excellent opportunity. His book is not just weak in content and rather limp in its

analysis; worse, it is a book apparently based almost entirely on publicity brochures and official handouts. Probably the best part is the introduction where Zahlan allows himself some critical consideration. However, from that point onwards, the book consists of straightforward description, potted history and dubious statistics.

The opening chapter presents a general view of the growth of scientific activity in the Arab World. Zahlan uses three basic sources for his information: UNESCO's *List of Scientific Papers Published in the Middle East (1948-1955)*, the now defunct *Arab Science Abstracts (1973-1975)* and *Who is Publishing in Science*. I would not be able to say anything about Arab science on the basis of these sources. Further I do not believe, as Zahlan does, that "scientific productivity measured in terms of publications of academic institutions is highly correlated with their scientific standing as assessed by leading scientists; it is also related to other outputs such as inventions, patents and the technological performance of the economy". These sorts of criteria for scientific productivity may be applicable to highly developed economies with sophisticated scientific infrastructures, but not to developing economies where scientists have more pressing concerns than

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publication. Zahlan himself is aware of the shortcomings of his methodology. However, no one is really any wiser at the end of the exercise.

As Egypt has the most highly developed scientific infrastructure in the Middle East, Zahlan appropriately devotes a whole chapter to the country. It is very much a historical discussion that traces science development in Egypt from 1951. An attempt is made to chart the development of scientific activity by measuring the increases in BSc and PhD degree holders (what is an Egyptian PhD worth, in real scientific terms, anyway?). Most of the statistics are taken from government ministries and technical institutes and no attempt is made to indicate the level of reliability of the figures. After Egypt, scientific activities in "selected countries" are presented: five pages on Kuwait, just over two on Iraq, less than a page on Saudi Arabia — which has one of the most rapidly expanding scientific bases in the Middle East, with astronomical sums being spent on science and technological development — and a half-page on Syria. Is that all that is happening in these countries and in the Middle East as a whole? Is nothing going on in Sudan, Algeria, Tunisia and Jordan?

After a similarly patchy and brief treatment of scientific manpower, we reach the last three chapters on funding, international and regional cooperation, and science policy, where at least an attempt has been made to be more thorough. The chapter on funding does manage to bring out both the channels being developed to fund scientific research and development and the resources available to capital-rich and capital-poor Arab states. The chapter on international and regional cooperation amounts to little more than the minutes of meetings of the Conference of Ministers of Arab States Responsible for the Application of Science and Technology to Development, and relies heavily on national papers submitted by Arab states to the recently held UN Conference on Science and Technology for Development. It is certainly not scholarship, neither is it good journalism, but it works as an account of recent history. This is also true of the chapter on science policy; here the commentary suffers by uncritical reproduction of material from brochures and annual reports such as that of Cairo's National Research Centre.

So, what value can one place on *Science and Science Policy in the Arab World*? The book has little of value to say about science policy, and even less about science, in the Middle East. But the book works, to a certain extent, as a history of science in the Middle East in general, and Egypt in particular, during the 1950s and 1960s. It is surprising that Zahlan has nothing much to say about recent — post-1975 — developments in science and technology. He seems to have overlooked the controversies about "Arabization" of

science, planning and developing technical institutions and universities, scientific bureaucracies and the debate on Islamic science. Perhaps these omissions are deliberate, but some discussion of these issues would have saved him from the accusation that the book is remarkably boring. Perhaps Zahlan feels that he has

said it all elsewhere in one of his many excellent publications. If this is so, then why write such an empty book? □

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Landau in retrospect

H.B.G. Casimir

Landau: A Great Physicist and Teacher. By Anna Livanova. Pp.217. (Pergamon: 1980.) £10, \$22.50.



Landau in 1936

LEV Davidovich Landau (1908–1968) was a brilliant theoretical physicist, an outstanding teacher and a striking personality, with an influence spreading far beyond the circle of his students and co-workers; his merciless criticism may have antagonized some of its victims, but he was most helpful and encouraging to anyone he considered worth helping. These characteristics are clearly brought out in Anna Livanova's well-written book. Although it is neither an exhaustive biography nor a critical appraisal of the whole of Landau's contributions to physics, the author has succeeded admirably in re-creating the image of this great man and in explaining to a general reader his ways of working and teaching.

The book opens with a brief biography. Landau was born at Baku and entered the university there at the age of 14. In 1924 he moved to Leningrad, graduating in 1927. Livanova gives a short but lively description of his student days. He learnt a little from his professors, quite a bit from discussions with fellow students — but most just by himself.

In 1929 he set out on an extended visit to western Europe and England. He went to see Pauli at Zürich, collaborated there with Peierls and wrote his famous paper on

diamagnetism (the description of which, by Livanova, leaves something to be desired). At Cambridge he met Kapitza, the beginning of a lifelong friendship, but of even greater influence on Landau were his contacts with Niels Bohr at Copenhagen. Livanova reports that Landau later regarded Bohr as his one and only teacher. That may seem surprising; I cannot think of two prominent physicists who differed more widely in their approach to teaching. Livanova calls attention to this difference, but in my opinion she does not sufficiently stress this point. I believe Bohr's influence was so important because his way of looking at physics was complementary to Landau's self-taught virtuosity. Landau had far more in common with Pauli in that they possessed comparable intellectual power and mathematical skills, and both could on occasion be redoubtable critics. Even so, there was a profound difference in their choice of subjects.

In 1932 Landau became head of the theoretical division of the Ukrainian Physicotechnical Institute at Kharkov. There he began teaching in earnest, collaborated with the experimentalists — especially with Shubnikow who had set up a cryogenic laboratory — and published a number of important papers. He left Kharkov in 1937 for Moscow and there he remained as head of the theoretical division of Kapitza's Institute of Physical Problems until his death in 1968; he always refused to become head of an institute of his own.

After a serious motor car accident in 1962, Landau became practically an invalid. One can sympathize with Anna Livanova in not entering into details concerning these later years, but I find it regrettable that, although she hints at difficulties at Kharkov, she does not mention that Shubnikow was arrested and never heard of again, and that Landau spent about one year in prison in 1938 and 1939 and might have perished but for Kapitza's courageous intervention.

For me, the most fascinating chapter is that concerned with "The School of Landau". This shows Landau at the height of his powers and gives a lively picture of his particular style and methods.

About half of the book is devoted to a description of Kapitza's work on the superfluidity of liquid helium and Landau's theoretical work in this field. The author preferred to consider one important and characteristic contribution of Landau's in detail instead of discussing superficially the whole of his work, and in

this she has been most successful in epitomizing the essence of Landau as a scientist. I have only one objection. No mention is made of the analogous and simultaneous experimental work of Allen and Misener at Cambridge, or of the theoretical work of F. London and of Tisza, who predicted second-sound several years ahead of Landau. The work of Landau was hardly influenced by these parallel developments, but the reader should know of them and that Landau's work, important though it was, was neither the only nor the final step towards a theory of superfluidity.

The final chapter, "Dau Away From Physics", recounts some amusing anecdotes but is hardly profound analysis. When I knew Landau at Copenhagen in 1930 and 1931 he was in a state of transition from shyness and reticence to the sociable and self-assured man of later years. He was then already classifying all things. Physicists, people in general and girls in

particular, books, poems, motion pictures, they all received marks from one to five (one the very best, five the worst and three just acceptable). Such grading also entered into his discussion of human relations. A couple where the man was a five, whereas the wife ranked a full three was unsatisfactory and should be broken up. In retrospect such considerations seem to me the immature and not even very witty self-defence of a sensitive and vulnerable man. Livanova takes them more seriously. In those faraway days Landau was not a happy man. Livanova mentions his claim that by his rational approach to human problems he succeeded in teaching himself to be happy. Did he really? I wonder. □

H.B.G. Casimir studied theoretical physics at Leiden, Copenhagen and Zürich, worked in low temperature physics at Leiden and later joined the Philips Company at Eindhoven. He was for several years President of the European Physical Society.

he shared the 1959 Nobel Prize in physics with Owen Chamberlain for the discovery of the anti-proton.

This book is based on lectures in which, as he says, "I tried to show not only the main discoveries but also the way they were reached, the personalities of the leading physicists and the errors committed before the right path was found". A prospective reader should not be misled by the title: the book is about the development of atomic, nuclear and elementary particle physics and "... does not pretend to be a history of modern physics. It is, rather, an impressionistic view of the events as they appeared to me during my scientific career ...".

Segrè gives fascinating accounts, from his perspective, of the discovery of the electron, X-rays, radioactivity; the old and new quantum theories and special relativity; nuclear structure and nuclear energy; particle accelerators and high-energy physics. The discussion is quite ample until about 1960. More recent developments, and accounts of related areas of physics, are treated in much less detail. For example, quantum electrodynamics, lasers and masers, the Mössbauer effect, superconductivity, astrophysics and biology are crowded into one chapter of 20 pages. In a final chapter, "Conclusions", Segrè points out trends toward greater specialization, industrialization, abstraction, and growing ties with technology in the current development of physics.

While an attempt is made to make the achievements of the major physicists "understandable to the layman", "Some knowledge of physics ... is necessary". Most formulae, however, are relegated to ten appendices ranging from "Stefan's law; Wien's law", to "Quantum Mechanics in a Nutshell".

Most semi-popular survey books of this type seem to be written either by theoretical physicists or non-physicists, and tend to overemphasize theoretical achievements and/or adopt an overawed attitude towards modern experimental techniques. It is therefore valuable to have a book written by such an eminent experimentalist. While he does not neglect the theoretical developments or the theorists, there is a better sense of balance, and of the interplay between experimental achievement and theoretical advance, than in similar books I have read. Since it is an avowedly personal account, Segrè does not hesitate to give his evaluations of the styles of work and personalities of the physicists he is discussing, or to illuminate the text with personal anecdotes and reminiscences. The book is also enlivened by numerous well-chosen illustrations, which really add a great deal of impact to the text. A reader comparing photographs of laboratories and sketches of experimental set-ups in the first few and in the last few chapters, for example, cannot avoid being struck by the growing industrial-

Emilio Segrè on physics and on physicists

John Stachel

From X-Rays to Quarks: Modern Physicists and Their Discoveries. By Emilio Segrè. Pp.337. (W.H. Freeman: 1980.) Hardback \$20, £11.80; paperback \$9.95, £5.40.

EMILIO Segrè is one of that group of extraordinarily gifted physicists that gathered around Enrico Fermi in the late 1920s, a

group whose members contributed so much to the development of nuclear and elementary particle physics in the ensuing decades. Like Fermi, Segrè came to the United States in 1938 and worked on the A-bomb project during the Second World War. After the War he returned to Berkeley, where he worked primarily in high-energy physics. An experimentalist,



Eight Nobel prize winners at the 1960 Rochester meeting. From left: E. Segrè, C.N. Yang, O. Chamberlain, T.D. Lee, E. McMillan, C.D. Anderson, I.I. Rabi and W. Heisenberg.

ization of experimental research in particle physics, also apparent from the text:

With a pun of dubious taste, I could say that it is no longer sufficient to be a Rutherford, but one must be a Rutherford-Ford, meaning that the physicist must have at least some of the qualities of an industrialist and of a businessman [p.294].

Clearly, Segrè identifies "the physicist" here with the elite of the scientific community. He does not note that if some scientists are to be industrialists and businessmen, this implies that many other scientists and technicians must be workers and wage labourers. To carry his pun a step further, today there is a Reuther-Ford division among scientists (Walter Reuther was the head of the US Auto Workers trades' union).

The comments of a leading physicist such as Segrè on men and events, his views on the development of physics and its place in the scheme of things have an intrinsic interest. But the question naturally arises: how reliable is such an unashamedly personal account? I have the impression that, overall, it is a rather reliable source of information, but have only checked the chapter on Einstein with any care. Judgements of personality will naturally tend to differ. Against Segrè's view of Einstein:

He was not averse to playing the role of the great scientist; clearly, he enjoyed it. Perhaps this explains some of his affectations, his strange manner of dress, and some habits that may have been for show. After all, he was an admirer and friend of Charlie Chaplin [p.97].

one might want to set that of Leo Szilard, who was more closely associated with Einstein:

He is a man as free from vanity as I have ever seen. I have heard him talk to an audience of a thousand in German where he was at his best, and he talked to them as he would talk to a few friends gathered at his fireside . . . If you meet him you are struck with his great modesty and his great simplicity of heart [*Leo Szilard: His Version of the Facts* (MIT Press, 1978) p.12].

As to biographical information, the chapter is fairly accurate, but I must report that there are several errors. For example, Einstein's academic career between 1908 and 1912 is incorrectly given on p.88, which also speaks of Einstein as disturbed by "the anti-Semitic atmosphere" in Prague at that time. The account of Einstein's theories is generally quite good, although Segrè gives more of an operationalist twist to Einstein's development of special relativity than I think is justified. More serious is the statement on p.95 that the experimental effects predicted by general relativity "are small and difficult to observe, so that even now there is no absolute and unequivocal

confirmation of the general theory of relativity". While certainly true, it seems to imply that Segrè believes that some other theories have been absolutely and unequivocally confirmed. This and other statements (for example the first paragraph of p.292) make it clear that philosophical problems of physics are not Segrè's strong point.

No account of the development of nuclear physics can avoid some discussion of the development of nuclear weapons, and the impact of this development on the modern world as well as on the physics community itself. Segrè gives such an account, and makes a number of interesting comments on the personalities and roles of J. Robert Oppenheimer and Ernest O. Lawrence, for example. His stance is that of an enlightened member of the US scientific establishment; one cannot find any searching criticism of either the scientific or political establishments here. His account would have to be supplemented from other sources by anyone seeking a thorough understanding of the origins of our present nuclear predicament. I do not mean to imply by this that Segrè is not well aware of the problem. In the few pages he devotes to "the influence of science on the human condition", as he puts it, he states his views:

. . . science enhances human power. It also permits (at least approximately) anticipation of the consequences of certain courses of action. However, the process of decision at both the individual and the state level is dictated not by science but rather by obscure factors that I understand only dimly. They seem to me to be largely irrational, possibly dictated by behavioural forces, evolutionary drives, or subconscious demons. We thus see courses of action that to an outside observer appear totally irrational and destructive in their consequences. The armament race is an outstanding example. Because science enhances human power, it makes these foolish pursuits more and more dangerous, so much so that they may imperil the survival of the species . . .

While the scientist has the specialized knowledge of his discipline, on other subjects he is pretty much prey to the same dark forces as is anybody else. His training and education may help him to overcome some of his irrational urges, but the idea that the objective, cool scientist is above the crowd is fallacious. This should be recognized by the scientists and by the public at large. Scientists are not priests of a magic religion [pp.288-289].

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Nuclear technology for the layman

Malcolm C. Scott

Unlocking the Atom: A Hundred Years of Nuclear Energy. By Malcolm Longstaff. Pp. 175. (Frederick Muller: London, 1980.) £7.95.

THE story of the development of nuclear energy is striking, both for the intellectual excitement which it has generated as well as for the intense political and moral arguments which have surrounded its use for weapons and for peaceful purposes. Yet, paradoxically, there have been few books which have attempted to cover these developments, particularly the technical aspects, in a way which makes them accessible to the general reader.

Despite the disclaimer in the preface — "... all I have been able to give is a sketchy account of some aspects, and particularly those which interest me most" — the scope of the book is broad. It starts with the discovery of uranium, radioactivity and fission and discusses the work leading to the two atomic bombs dropped on Japan. The post-War development of nuclear reactors for plutonium production is then covered, leading on to the start of the non-weapons orientated reactor programme. The main features of the principal power reactors in use around the world are

outlined, followed by chapters on uranium and its fabrication into fuel (including the use of lasers for enrichment), fuel use and reprocessing, and radioactive waste disposal. There are then separate chapters on safety, on energy and the place of nuclear power, and on other uses of nuclear energy. Finally, in "Looking Ahead", the author touches on some of the current arguments relating to nuclear power (for example, the question of the blackmail value of plutonium and the possible role of thorium in separating the peaceful and non-peaceful uses) and outlines the principles of nuclear fusion. Throughout the book there are well-chosen photographs and numerous other figures.

The author keeps to his intention to give "little chemistry and no mathematics", yet, nevertheless, manages to provide a comprehensive technical coverage of the subject. In doing so he defines the terms which he uses in a non-technical way, so that the lay reader should not find it necessary to read with a technical dictionary at his elbow.

There are a few inconsistencies — for example, the abundance of uranium-235 is given variously as 1 part in 140, 1 part in 139 and 0.3% (1 part in 333: this is certainly a

typographical error). Nevertheless, they are few, and the general tone of the text is one of technical correctness and authority. Yet, despite these undoubted virtues, there is something lacking: it is simply that the author has not succeeded in making the field as enthralling as he found it during his 24 years with the United Kingdom Atomic Energy Authority. Instead, one is left with the uneasy feeling that the book reads like a succession of the carefully worded, technically correct, but bland handouts favoured by public relations officers, particularly in the nuclear industry. The sense of excitement aroused by the initial discovery of fission is missing, as is any sense of the enormous technological achievement in harnessing nuclear power.

After all, the reason why nuclear power bears the brunt of the anti-technologists' onslaught is precisely because it is seen as *the* high technology, an almost unique amalgam of science and engineering. Yet none of this emerges. Everything is under control, doubts are smoothly assuaged and technology rules supreme.

Nevertheless, for the reader who is prepared to accept these limitations, the book provides an accessible and comprehensive survey of the nuclear scene at a level which invites a wide readership. □

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Another delicate issue concerns the need for a clear definition of life. Superficial criteria such as the ability to reproduce, response to environment and so on are also displayed by systems that are normally regarded as inanimate, so Feinberg and Shapiro adopt a sort of global definition wherein life is manifested through the activity of a biosphere; that is, one should look to the highly organized and complex structure of interlocking organisms as an unambiguous indicator of life.

At the end of the day we are still left with the depressing fact that the discovery of extraterrestrial biospheres is unlikely to occur in the twentieth century, so all books of this sort really amount to little more than speculation, or at best educated guesses. Nevertheless, there is a real need for us to examine fresh perspectives of mankind and his place in the Universe. With that in mind, I found the book entertaining and generally informative.

In contrast to this ambitious work, *Earth and Cosmos* by Robert Kandel is more modest in aim though wider in scope. The author also provides a cosmic perspective of mankind by discussing in detail a whole range of physical processes that are relevant to the structure of the Earth and its immediate environment. This book is full of fascinating information, ranging from continental drift to the pollution of the atmosphere. There is an extensive discussion of both meteorology and climatology, and a detailed review of the Earth's motion. *Earth and Cosmos* makes good reading for non-specialists who want to know more about the planet we live on. □

Paul Davies is Professor of Theoretical Physics at the University of Newcastle upon Tyne.

Life as we know it: does anyone else?

Paul Davies

Life Beyond Earth: The Intelligent Earthling's Guide to Life in the Universe. By Gerald Feinberg and Robert Shapiro. Pp.480. (Morrow: 1980.) Hardback \$14.95; paperback \$7.95. *Earth and Cosmos.* By R. S. Kandel. Pp.270. (Pergamon: 1980.) Hardback \$30, £13.50; paperback \$14.90, £6.95.

Life Beyond Earth, proclaims the publisher's blurb, "is the result of a three-year collaboration between a theoretical physicist and a biochemist . . .". That sounds like a recipe for disaster, but the end product is remarkably coherent, if a little prolix. It is also somewhat pretentious, because it presents a range of ideas, varying from uncontentious standard biochemistry to the most outrageous and bizarre speculations, in a deceptively uniform and scholarly format.

It is, of course, the outrageous ideas that make this book such fun to read. The authors pin their colours firmly to the mast in Chapter 1: "We believe that most other attempts . . . have not been sufficiently imaginative in examining the possibilities for extraterrestrial life". To remedy this state of affairs, the reader is invited to consider the astonishing prospect of living creatures inhabiting the most unlikely of habitats — wallowing in the molten interior of the Earth, bobbing about inside the Sun, crawling over the surfaces of neutron stars, or floating serenely and nebulously in interstellar space. This is all good sci-fi stuff, but my main misgiving is that while the mere existence of a source of free energy and a mechanism for self-organization are certainly necessary conditions for the appearance of some form of life, can we really believe, as the authors assume, that they are sufficient?

A related problem to the happy prospect of a Universe teeming with exotic life forms is that it is far easier to believe in the evolution of intelligence, once life

has actually gained a foothold, than in the initial appearance of living things. Yet if intelligence abounds in the cosmos, we would expect it to be conspicuous. Where is the alien technology, some of it presumably billions of years more advanced than ours? Unfortunately, Feinberg and Shapiro almost completely ignore the subjects of intelligence and alien communities, so do not attempt to face this central issue.

It would be misleading, however, to over-emphasize the bizarre in this book. The authors provide a valuable service in, for example, drawing attention to the distorted public image of the Viking experiments on Mars, popularly believed to have excluded the possibility of life there. In fact, as the authors' careful analysis shows, the results were ambiguous, and the experiments in any case left a lot to be desired in their underlying assumptions about Martian biology.

One can also be persuaded by their argument that the search for extraterrestrial life contributes hugely to the motivation for the general exploration of space. Public disappointment that space probes have not yet positively encountered even the tiniest form of life has contributed to the widespread disillusionment with these expensive enterprises. Yet the most likely abode for life in the Solar System — Jupiter — has still to be closely explored.

Inevitably, for a book that tackles a subject for which no known subject matter yet exists, *Life Beyond Earth* contains liberal doses of philosophy. Specially singled out for attack are those whom the authors dub as "carbaquists" — biochemical faint-hearts who believe that life based on the chemistry of carbon and water is the only possibility. As a physicist, the carbaquist viewpoint has always seemed to me chauvinistic; biochemists are doubtless more conservative.

Cosmic questions

Joseph Silk

The State of the Universe. Edited by G.T. Bath. Pp. 199. (Oxford University Press: 1980.) £8.95, \$24.95.

DESPITE its obscure origin and intemperate past, the Universe has made a good recovery. Conditions have stabilized over the past several eons, and practically all observers now agree that a recession is with us for some time to come. However the long-term outlook remains controversial — some predict that the rate of inflation will eventually drop, heralding the onset of a long era of deflation; other forecasters, perhaps a majority, maintain that the inflation rate will hold steady into the remote future. A vocal minority even persist in finding evidence that the inflation rate is accelerating.

This situation must seem familiar to the student of economics. Likewise, cosmologists also have their differences. It

may seem strange to the layman that experts should disagree on whether the Universe will perpetually continue to cool down, to attain inexorably the ultimate energy crisis, or whether it is destined to overheat and implode into a brilliant fireball, hotter and more intense than anything imaginable by human beings. The uncertainty arises because the currently available indicators are often contradictory; the cosmologist has considerable scope for rejecting evidence that may not fit his model, especially if the evidence is incomplete and tentative. A choice still remains between the "Heat Death" of the Universe and the "Big Squeeze".

Yet our knowledge of the Universe is increasing at an unprecedented rate. The availability of observatories in space has enabled astronomers to study the Universe over much of the electromagnetic spectrum that is inaccessible from ground level, from gamma-rays to infrared radiation. And modern technology has revolutionized ground-based observing. The caricature of the earnest astronomer peering through a telescope in a cold, dark observatory dome is a myth that has long been displaced.

The modern astronomer punches in coordinates on a computer console and views the stars on a video display in a brightly lit room crammed with sophisticated electronic instrumentation. The aim is to probe ever deeper into the mysteries of the Universe, by furthering our understanding of the structures within it, from stars to galaxies, alone and in their great clusters.

Astronomers are now able — albeit barely so — to trace images of ordinary galaxies so distant that their light was emitted before the Earth was formed. In principle, with sufficient information about such systems, one could directly infer their distances and decide whether the rate of expansion of the Universe has changed significantly over this time-scale. The future of the Universe could then be predicted unambiguously. It seems likely that within the next one or two decades, provided that governments continue to make the necessary commitment to science, advances in technology, both ground-based and in space, will enable detailed studies to be made of remote galaxies at the observable edge of the Universe.

The State of the Universe, based on the Wolfson College Lectures given at Oxford in the Spring of 1979, provides a fascinating and highly readable account of several of the major developments that have taken place in astronomy and cosmology over the past decade. Eight leading scientists who have played key roles in many of the discoveries cover a diverse array of topics, ranging from G.E. Hunt on the exploration of the planets to D.W. Sciama on the origin of the Universe. Especially memorable is the contribution by R. Penrose on black holes, for its lucid account of space-time singularities. M.J.

Rees writes on galaxies, their nuclei and their origin, and R.J. Tayler describes current views on the origin of the chemical elements. Hunt's beautifully illustrated chapter is one of the highlights of the book, providing a full and timely account of the newly acquired knowledge of the planets from Mercury to Jupiter. Remaining chapters include D.E. Blackwell on the stars as suns, K.A. Pounds on the X-ray Universe and F.G. Smith on new ways of seeing the Universe. Geoffrey Bath is to be commended on having co-ordinated an extraordinary lucid array of timely contributions from a group of the most eminent, and certainly among the busiest, of British astrophysicists.

On reading *The State of the Universe* one cannot fail to be impressed by the immense

vistas that the explosive progress in astronomy has revealed. Much is poorly understood: indeed, a radically new approach to physics may be required if we are to discover the origin of the Universe, for example. But enough has fallen into place for us to be confident that our theories enable us to understand how much of the Universe entered into its present state. Prediction of its future evolution now becomes feasible. We can already do this for stars: it may not be long before enough data is at hand to determine definitively the future of the Universe, no less. □

Joseph Silk is Professor of Astronomy at the University of California, Berkeley, and author of *The Big Bang*, published earlier this year by W.H. Freeman.

Tuning in to astronomy

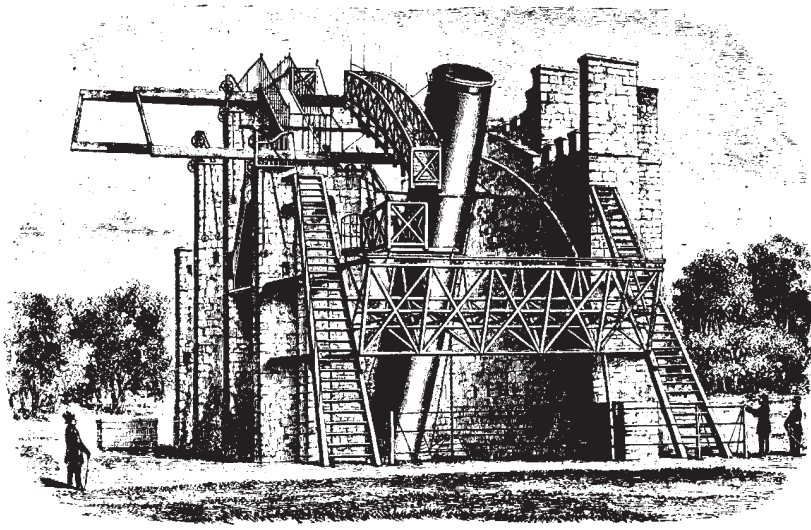
David W. Hughes

Starseekers. By Colin Wilson. Pp.271. (Hodder and Stoughton/Doubleday: 1980.) £10.95, \$15.95.

COLIN Wilson, the Colin Wilson who wrote *The Outsider*, *Introduction to the New Existentialism*, *Strange Powers* and a host of other titles, has now turned his attention to astronomy. He has written a fascinating account of how he thinks astronomers tick today, did tick in the past and should tick in the future, if, that is, they ever wish to solve the "fundamental question". What is the question? Bertrand Russell once said that the aim of philosophy is to understand the Universe. Wilson urges us to go a step further. The question is not just "what is the Universe?". It is "what is the *purpose* of the Universe?". Purpose, a word that makes all good scientists shudder. How should we — dry, dusty, intellectual

astronomers, tied to our telescopes, computers and respectable thought processes — delve into the understanding of the purpose of things? Wilson reveals his answer by frequent use of such phrases as "flashes of second sight", "supra-logical processes", "paranormal" and "intuitive insight". We are not told to abandon our scientific principles, we are simply encouraged to recognize that they are incomplete. There is always more than meets the eye.

The book divides into three sections. The first is a review of ancient cosmologies. Why should our ancestors build Stonehenge, what was the real purpose of the pyramids, did the ancient Egyptians know about the precession of the equinoxes? Wilson refers often to bicameralism and has obviously been much affected by Julian Jaynes's book *The Origin of Consciousness in the Breakdown of the*



Lord Rosse's giant six-foot reflector at Birr Castle in Ireland

Bicameral Mind. The brain is apparently split into a left half which is the home of rationalist, logical and scientific thought and a right half which houses artistic feelings and intuitive insights. Human development has led to a changeover in the dominant section. Civilization has suppressed the messages from the right brain and allowed the left brain to take over.

The second section of the book deals with the life histories and scientific achievement of some of the great renaissance scientists, Copernicus, Brahe, Kepler, Galileo, Newton and Hershel. The ghosts of Koestler's *The Sleepwalkers* and Dreyer's *A History of Astronomy from Thales to Kepler* haunt these pages.

The third section brings us firmly to the present day and traces the acceleration of

astronomical discovery that has occurred since Einstein's gravitational theory and the advent of quantum mechanics. Planetary exploration, radio astronomy, big bang cosmology, black holes, the origin of life — all are touched upon. Throughout the text echoes the Wilson message that there is more to our astronomical Universe than science can understand. The investigators must try and tune into this ethereal suprahuman influence on our destiny in a manner similar to that used by our ancient ancestors.

I enjoyed reading this book. It was fun. The style is excellent, the production standard and the illustrations are superb. But I continually had an uneasy feeling. It is an axiom that you should not believe all that you read; the reader of this book should not, and Colin Wilson should not

either. He has a regrettable tendency to regard the printed word in the same light as the tablets of Moses. Many eminent authors are quoted — Hoyle, Koestler, Motz, Taylor. When discussing Hoyle's *Lifeclock* and *Ten Faces of the Universe*, Wilson states that "No-one is going to quarrel with what they say". What? Scientists always question what other people say. The scientists such as Galileo, Kepler and Newton who are discussed in Wilson's book thrived on it. So should the readers of *Starseekers*.

But still, I congratulate Colin Wilson. Once you pick the book up it is hard to put it down. Interesting thoughts and problems sparkle from every other page. □

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James Six and his thermometer

W. D. Hackmann

The Construction and Use of a Thermometer. By James Six. Introduction by Jill Austin and Anita McConnell. Pp.123. (Nimbus: London, 1980.) £15.

THIS small book reproduces the papers of an almost totally forgotten eighteenth century man of science, James Six (1731 – 1793), the descendant of a refugee Walloon family of silk weavers who settled in Canterbury during the reign of Elizabeth I. He was one of a score of amateur scientists who, through their individual small contributions, made scientific progress possible during the eighteenth century.

His tastes were typical of the contemporary intelligensia; painting, astronomy, electrical experiments with the new-fangled frictional electric machines, and meteorological observations. He invented a maximum and minimum self-registering thermometer in 1780; a worthwhile contribution for which he was awarded a Royal Society Fellowship in 1792. His thermometer, in which the extremes of temperature were recorded by sliding indexes, has survived as a popular domestic instrument. With it he observed the night-time inversion of temperature, a phenomenon not explained by meteorologists until the following century.

The largest portion of the book is taken up with a reproduction of Six's *Construction and Use of a Thermometer*, published in 1794, and essentially a summary of his three papers on thermometry published in the *Philosophical Transactions* with the addition of a chapter on the deep-sea use of his instrument. Eight pages are devoted to his other scientific communications. The bulk of these are his seven letters to the *Gentleman's Magazine*, a popular organ

for the amateur scientist. In 1770 he described a comet later known as Lexell's Comet. Its orbit was calculated by the American astronomer David Rittenhouse and Six's observations largely agreed with this. In 1771 and 1781 he recorded the appearance of two other comets. Other topics dealt with were the 1784 heat wave, William Herschel's recently discovered "Georgian Star" (Uranus) and a severe frosty spell in 1789. Also reproduced is a letter from the archives of the Cambridge University Library, written in 1785 by Six to a student friend of his son on the use of his thermometer. This series is terminated by a charming obituary of Six, also from the *Gentleman's Magazine*.

The only Six-type thermometer known before the researches of Austin and McConnell was the one in the Museum of the History of Science at Oxford. However, it is not contemporary, having probably been made in the 1820s for Charles Daubeny whose chemistry laboratory was housed in the present basement of this Museum. The authors have identified 26 thermometers made by Six and now part of the King George III Collection at the Science Museum in London, and another specimen of obscure origin at the Copernicus Museum in Rome. These are described in some detail and the subsequent development of the instrument is also given.

All in all, this small, attractively-bound volume not only adds a little to the history of thermometry, it also gives us another glimpse into the world of eighteenth-century men of science. □

W. D. Hackmann is Assistant Curator of the Museum of the History of Science, University of Oxford.

IMAGE
UNAVAILABLE
FOR
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REASONS

Mathematics for the non-mathematician

P. T. Saunders

Handbook of Applicable Mathematics. Chief editor Walter Ledermann. Vol. I *Algebra*. Edited by Walter Ledermann and Steven Vajda. Pp. 532. (Wiley: 1980.) Subscription price for core volumes £27.50, \$75 each, single volumes £32.50, \$85.

UNLIKE their colleagues in physics, workers in the biological and social sciences have generally received very little training in mathematics. Few of them know more than a bit of calculus and some elementary statistics. As a result, they can find themselves totally unable to understand the increasing number of papers in their fields which employ more sophisticated mathematical techniques. Nor is it easy for even the most determined of them to do anything about this. It can be exceedingly difficult for a non-mathematician just to discover where to look up something, and even then he may be not very much further ahead. Mathematics is a cumulative subject; every new idea tends to depend on many that have come before. So he is likely to find that the explanation of the concept he is interested in is in terms of several other concepts which are equally unfamiliar. And as if that were not enough, at least some of these may originate in a different branch of the subject and not even be defined in the book he has consulted.

The *Handbook of Applicable Mathematics* represents an attempt to help "users of mathematics who are not professional mathematicians" when they find themselves in this awkward position. On completion it will consist of 16 volumes. The first six, called "core" volumes — *Algebra, Probability, Numerical Methods, Analysis, Geometry and Combinatorics, and Statistics* — are intended to cover all the mathematics the non-specialist is likely to encounter. There will also be ten "guide books", showing how mathematics is applied to different fields such as chemistry, economics, sociology, management, medicine and so on.

According to the editors, the aim of the *Handbook* is that "professional adults" needing to understand a particular mathematical idea will be able to find in it "just what they want to know". They have therefore tried to make the articles self-contained, to allow the reader to turn directly to the topic in question, rather than start at the beginning of the book. There is an elaborate cross-referencing system throughout the entire *Handbook*, so that any unfamiliar term or result can be located quickly and without searching through other works. They also claim to have "gone to great lengths to ensure that no branch of mathematics is omitted which is useful, and conversely that none is included which is not".

In some respects, the impression given by *Algebra*, the first of the core volumes

and the only one so far available, is encouraging. The general standard of writing and exposition is good, and the authors have kept in mind the desirability of explaining to the reader in plain language what is going on and what some of the definitions "really" mean.

Viewed in the light of the claims made in the introduction, however, some important shortcomings appear. While the explanations are clear and often illustrated by examples, the pace often seems too fast for a newcomer to the topic, and there are no exercises. There are inconsistencies between the chapters with regard to the amount of detail included; this is always a problem in multi-author texts but more could have been done to combat it, especially in such an ambitious work. Further, the selection of topics does not appear to have been made with the care and ruthlessness promised in the introduction; perhaps an analyst might agree that the long account of decimal expansions (without, incidentally, any real mention of other bases) is necessary, but two pages on quaternions seems an avoidable luxury.

The real problem with this book, however, is that in trying to cater for all levels of mathematical competence in one work the editors have set themselves an impossible task. There is a limit to the speed with which mathematics can be assimilated. Most of us can learn a new mathematical idea if it is clearly explained to us in language we can understand. And we may even manage to learn a second new idea based on the first. But before we can grasp a third new idea, and a fourth, we generally need some time and practice to enable us to become familiar with what we have just been taught. Many of the less essential topics which are included in mathematics courses are there for just that purpose. If we try to go on before we have allowed the first ideas to sink in, we are unlikely to understand the later ones, because they will be being explained in terms of ideas which are not yet a secure part of our mathematical vocabulary. So an explanation which is suitable for someone who has a good background in mathematics cannot be made suitable for someone who has not just by referring the novice back through a chain of earlier explanations.

So far as can be judged from the first volume and a proof copy of *Probability*, and without seeing any of the guide books, the *Handbook of Applicable Mathematics* will be of most value to those who already know rather more than the average amount of mathematics. They will find it a useful aid, but if it had been designed specifically for them it would have been a lot better. As it is, it tends to fall between two stools, with too much detail for reference and not enough for real learning, and despite its

virtues many potential users may not feel it worth the considerable outlay. As for someone with only a minimal previous knowledge, he is unlikely to find that the series will open the rich storehouse of mathematics to him, even with the effort the editors warn him will sometimes be required. He would do better to try to acquire a solid foundation from some of the good — and much cheaper — elementary textbooks which are already available. There is, as has been said before, no royal road to geometry. □

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Whither geography?

K. J. Gregory

Geography: Yesterday and Tomorrow. Edited by E. H. Brown. Pp. 302. (Oxford University Press: 1980.) £10, \$29.95.

THE 150th anniversary of the Royal Geographical Society provides the *raison d'être* for this volume. Founded in 1830, the RGS was third in the world following the establishment of geographical societies in Paris in 1821 and Berlin in 1828; like them its function included the encouragement of exploration and discovery, a tradition which has persisted to the present day.

Although the first professor of geography in Britain was appointed in 1833 at University College, London, the subject took firm root in Oxford and Cambridge, and between 1883 and 1924 the RGS gave grants to these two universities to foster its development. The Geographical Association, concerned with geographical education in schools, was founded in 1893, and in 1933 a group of geographers formed the Institute of British Geographers to provide an outlet for research publications because it was felt that the *Geographical Journal* had insufficient space for both research papers and accounts of exploration and travel.

Today, for the first time, both the President and the two Honorary Secretaries of the RGS are university geographers. Such strong links with university geography have not always featured during the course of the 150 years which are charted by T. W. Freeman in the first third of the book. Freeman concludes that the struggle for recognition of the subject has now been won; the way in which this was done and the subject recognized and established in education is explained in the following contribution by N. J. Graves.

To reveal the yesterday and tomorrow of geography as an academic discipline, the subject is divided into 12 subdisciplines,

each discussed by a different author. Inevitably, perhaps, they do not adopt a consistent approach. Some contributions are stimulating reviews which concentrate on major developments and prospects; W. R. Mead on the essence of the regional ideal, A. G. Wilson on the position of theory in human geography and Emrys Jones on the scope of social geography consider three aspects of the subject that have been prominent and partly sequential in geographical thinking during the past two decades. Other authors give a chronological summary of development in a particular branch of geography — geomorphology, land use survey, leisure and recreation, and medical geography — with passing reference to the role of the RGS. A third type of contribution provides a state-of-the-art summary of the approaches adopted by contemporary research schools; this is very effective in discussions on climate and on biogeography, tends to be somewhat compressed for historical geography, and embraces trends beyond the subject for surveying and mapping and in the chapter "Water as a Geographical Issue". Not all geographers will agree that this range completely portrays the current academic spectrum. In particular, one might have expected a consideration of philosophical approaches to the subject, and of urban geography which has been responsible for a very substantial proportion of the research output in human geography since 1960.

The overall impression of geography given by the book is that it is a subject not as disintegrated as the titles of the chapters might indicate. It is evident that more energy has been devoted to some branches, such as geomorphology, than to others, climatology for example. It is artificial to erect a barrier around a subdiscipline, and it is shown how the development of theory and of surveying and mapping, and of branches such as historical geography and medical geography, have flourished by contact with and exposure to proximal disciplines.

The debate as to whether the physical could, and should, separate from the human part of the subject appears in at least one incisive discussion, but it is apparent from a number of branches that contributions to practical problems associated with earth hazards, and social, recreation and leisure, and medical geography arise because the subject spans the interface between human activity and environment. The geographer thus has to be conversant with some techniques from the pure and applied sciences and others from the humanities and social sciences. This is at once part of the characteristic skill of the geographer. Also clearly emerging as a recurrent theme is the importance of spatial analysis — perhaps geography is really about maps, although the map may today be in the form of an equation, a satellite image or a data bank.

In the final thought-provoking chapter,

W. R. Mead, a former Honorary Secretary of the RGS, epitomizes geography as a synthetic subject in which the regionalists are closer to the heart of the subject than most. Whereas the regional ideal used to be the only crumb of integration that was offered, we now have further applicable links offered by the study of water, biogeography, land use, leisure and recreation, and medical geography. Perhaps geography tomorrow will find its integrity not solely dependent upon the classic regional approach and a book produced for the 200th anniversary could promulgate even closer liaison between the branches of the subject.

The editor introduces the volume as

being designed to do many things, among them to explain what is geography, what do geographers do and what use is geography. In answering these questions, particularly the second, the book is a great success. It is enjoyable to read and is extremely stimulating. Students and others should be encouraged to buy this book, but having read it they may find, like me, that an index would have been invaluable because the volume certainly deserves to become a standard work of reference. □

K. J. Gregory is Professor of Geography and Chairman of Department at the University of Southampton.

To boldly go. . .

Sarah Bunney

To the Farthest Ends of the Earth: 150 Years of World Exploration. (The History of the Royal Geographical Society 1830–1980.) By Ian Cameron. Pp.288. (Macdonald/E.P. Dutton: 1980.) £10.95, \$29.95.

I ASSUME it was primarily the shape rather than the subject matter that determined the prominent position of this vignette on a preliminary page of Ian Cameron's book in honour of the Royal Geographical Society, but it was an apt choice nonetheless. The engraving represents two important aspects of Victorian exploration — the appalling hardships endured by the explorers as they strove to satisfy their curiosity, and the disappointments and controversies that accompanied many nineteenth-century expeditions. In particular the picture draws attention to the sadly misguided preference of British Polar

explorers for man-hauling their equipment instead of using dogs. It was this policy, which received the Society's support for some 50 years, that contributed to repeated disappointments on Arctic expeditions and eventually to Captain Scott's defeat in the race for the South Pole in the early 1900s.

Ian Cameron, who had access to the Society's records while writing his book, is scrupulously fair in his treatment of this unhappy story and of the other difficulties that beset many of the expeditions in the Society's first 75 years. Personalities, warts and all, are vividly brought to life. Mr Cameron also gives a balanced account of the Society's more recent — and somewhat insensitive — handling of the choice of leader for the Everest expedition. In the event this expedition was a glorious success and it is, of course, achievement and not failure that this book is mostly about. There is plenty of solid, but never heavy description of the most important expeditions of the past 150 years, accompanied by excerpts from notebooks, dispatches and contemporary accounts in the Society's *Journal*.



All this makes for such fascinating reading that I would have preferred more of the highly readable text and fewer illustrations — even though many of the latter are delightful, particularly the polished sketches by Baines and the early photographs. My one serious complaint concerns the maps. It is ironic that, in this of all books, these are heavily drawn, inadequate and, in at least one case (the Musandam map on p.224), inaccurate. Furthermore the two contemporary maps included are almost illegible, they lack captions and it was only on reading the acknowledgements that I learnt of their source and date.

This book cannot be a comprehensive history of the RGS, and Mr Cameron has wisely concentrated on the expeditions to areas that have long been the favourites of armchair travellers — the Arctic and Antarctic, the Himalayas and Africa. New to me were most of the early explorers of Australia and the brave Pundits who secretly and at great hazard to themselves surveyed on foot almost the whole of the Eastern Himalayas in the 1850s to 1870s. Childhood heroes — Burton, Speke, Livingstone, Stanley, Nansen, Shackleton, Scott, Hunt, Hillary and Tenzing (but only one heroine, Florence Baker) are included. Mr Cameron also gives credit to many other explorers, less well known but equally deserving of fame, who doggedly helped fill in the blanks on the maps. I am only sorry that room could not be found in this catalogue of illustrious names for some



After the summit of achievement: Hillary and Tenzing after the first ascent of Everest, May 1953.

mention of the Arabian travels of Wilfred Thesiger and Freya Stark.

Mr Cameron brings readers up to date with accounts of some of the recent, increasingly scientific, expeditions that the RGS has supported — to the Mato Grosso (1967–1969), the Musandam Peninsula (1971) and the Mulu rain forest in Sarawak

(1977–1978), for example. The book ends with a chapter on the role of the Society today as it continues to advance geographical knowledge. It is a quieter role, without the glamour and heroics of the past, but no less important for that. □

Sarah Bunney is a freelance writer and editor.

Stonehenge and its times: a layman's and a scholar's view

R.J.C. Atkinson

The Enigma of Stonehenge. By John Fowles and Barry Brookoff. Pp.128. (Cape/Summit: 1980.) £6.95, \$19.95. *The Age of Stonehenge.* By Colin Burgess. Pp.402. (Dent/Biblio: 1980.) £12, \$25.

THESE are two very different books, which have in common only the name of Stonehenge in their titles. The first is the result of a most happy collaboration between an English novelist and an American photographer, both of genius, to give a unique picture of Stonehenge itself. The second is a sober and most scholarly interpretation (John Fowles would call it clinical) of the prehistory of the British Isles during the *flourit* of Stonehenge.

Fowles's short account begins with his own first happy visit to Stonehenge as a child, and with his last, less happy because the stones are now closed to the public. His summaries of the archaeological background and of the sequence of building can be faulted in detail by the pedantic specialist; but they are based on a wide and critical reading, and they are written with a delusive ease and with an informed humanity which puts to shame the earnest

but pedestrian locutions of most other recent writers about Stonehenge, myself included.

He asks: "What is Stonehenge for?". For me this is an unanswerable question, because I do not think that the mute material evidence of prehistory can tell us, except in a quite trivial sense, what people thought in the remote past, but only, up to a point, what they did. This is not to say, as Fowles hints, "a pox on all speculation"; but speculation and valid inference are two very different things, and must be distinguished, perhaps better than Fowles does.

In his longest chapter, "The Moon-Mirror", he perhaps accepts too easily some of the astronomical uses ascribed to Stonehenge by Hawkins, Hoyle, Newham and Thom. Moreover, he confuses the Metonic Cycle with the period of rotation of the lunar nodes, and falsely explains the position of the Heel Stone, as a possible marker for the mid-point of the azimuthal limits of most northerly moonrise, in terms of the latitude of Stonehenge. He also infers, quite incorrectly, that the absence of any discussion of astronomical theories from my own book *Stonehenge* (Hamish

Hamilton, 1956) was intended as a "monumental snub" to Hawkins, Hoyle and Thom. Far from it. My book was written in 1955, before any of these theories were published, and has since been reprinted only with appendices to bring the results of later excavation up to date.

Fowles's luminous text ends with an historical and personal appreciation of Stonehenge-in-the-mind, and not least in the mind of that eerie and disturbing seer, William Blake. He protests throughout against "a quite unnecessary polarity in twentieth-century society between pure science and impure speculation". This echoes what I wrote in *Nature* (265, 11; 1977). The science is far from pure, because much of the basic data are at best uncertain, and at worst corrupt. The speculation is likewise not impure, merely because it is speculation; but it is not inference compelled by the evidence of Stonehenge-on-the-ground.

Barry Brookoff's photographs, unnumbered and uncaptioned, match John Fowles's text in their sensitivity and imagination. No one has better frozen in print an image of Stonehenge. His

From *The Enigma of Stonehenge*

occasional use of a wide-angle lens gives a sense of spaciousness which the monument itself belies, though one which echoes some of William Stukeley's engravings of 1740. Occasionally a Sun or Moon has been added by photomontage for dramatic emphasis at far more than natural size. Not the least haunting of these photographs capture, as none has before, the texture of the surface of some of the sarsen stones, in which each beholder will see his own private vision.

This book, in words and images, will enlarge the consciousness of every visitor to Stonehenge, past and future.

Colin Burgess's book will likewise extend the thinking of every British prehistorian, and of colleagues abroad. It is a major advance in the synthesis of the new evidence which has become available, almost explosively, from excavations and the analysis of museum collections during the past 20 years for the period of 3,000 years from 3,200 BC, which corresponds roughly to the use of Stonehenge.

He divides this into five periods, each identified by a type-site, and each characterized in his view by specific practices or trends, in ritual architecture for worship or burial, and in the design and manufacture of artefacts. This is a convenient chronological device for avoiding the constraints of ill-fitting radiocarbon dates with their present state of uncertainty. He gives also, however, a list of 215 radiocarbon dates in their raw (uncorrected) form. One may ask whether these, when corrected, may not provide a better framework than a series of largely arbitrary periods which, because they are new, may be adopted and maintained long after they have ceased to be significant. He rejects, rightly, the old and now outmoded divisions of the conventional Neolithic and Bronze Age.

Burgess's main thesis is that tribal territories had already been fixed by the end of the fourth millennium BC, and that thereafter cultural change took place by the adoption of innovations across persisting tribal boundaries, with local adaptations increasing in proportion to the distance from the primary source. This is a possible model, though the one which rests on a number of quite unverifiable assumptions, and one which rejects explicitly the "invasion hypothesis" that has long been dominant in explanations of British prehistory.

In his proper desire to emphasize cultural continuity, however, he has

perhaps underestimated the impact of the Beaker people coming from across the North Sea and the Channel in the middle of the third millennium BC. Whether this was an invasion, an incursion or an immigration, or a series of any of these processes, on whatever scale, is largely a semantic question. What is evident is that there was a fairly rapid innovation in material culture, superimposed on native practices which survived by absorption. This cannot be explained except by an incoming from abroad, and a break in the continuity of native traditions. Burgess does admit, quite rightly, that at the end of the "Age of Stonehenge" there may have been an influx of foreigners who established the succeeding "Age of Hill

Forts", though they are far less well represented in the archaeological record than the Beaker people.

This is a book for specialists in British prehistory, and not least for university students. It is well illustrated by photographs of sites and objects. The numerous line-drawings of plans and artefacts have been rather over-inked and thus harshly reproduced, and the inclusion of north-points and scales is a little capricious. Minor defects apart, it is a major contribution to the understanding of a formative period of our prehistoric past. □

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The rediscovery of ancient Ebla

J.M. Munn-Rankin

EBLA: An Empire Rediscovered. By Paolo Matthiae. Translated by C. Holme. Pp.237. (Hodder and Stoughton/Doubleday: 1980.) £12.95, \$14.95.

THE excavation in 1974 and 1975, at the north Syrian site of Tell Mardikh, ancient Ebla, of a mid-third millennium palace with some 20,000 cuneiform tablets written in a previously unknown Semitic language was an event of outstanding importance for historians of early urban society in the Near East.

Prior to this discovery, archaeological and textual evidence for developments in Syria during the Early Bronze Age (c. 2900–2000 BC) was meagre. As compared with the earliest centres of civilization, Sumer and Egypt, relatively few Syrian excavations had penetrated below second millennium levels and of these most were stratigraphic sondages. At only a few major sites, mainly in the north-east, had more extensive excavation produced significant evidence of urban settlement. Literacy was attested only at Mari on the Euphrates where a Semitic language was written in the cuneiform script of Sumer. Of the population it could be said only that it was probably of mixed ethnic origin and that its social structure ranged from primitive nomadism to complex urbanism. It was, however, apparent that the urban civilization of Sumer, in existence by the second half of the fourth millennium, had

played a major role in the formation and subsequent development of Syrian civilization, the main impetus for the expansion of its influence being the need for the timber, stone and metal in which southern Iraq is deficient. As regards the political geography of Syria, a limited amount of information was provided by the records of Sumer, among the earliest being the campaign reports of Sargon and Naram-Sin of Agade (c. 24th and 23rd centuries BC) which list cities conquered on expeditions to the Mediterranean. Among them is Ebla.

This inadequate picture of the early culture and history of Syria is now being transformed by the excavations of Paolo Matthiae of Rome University at Tell Mardikh. In this report on their progress, he describes and assesses the significance of the finds made between 1964 and 1976. The site was occupied from the latter half of the fourth millennium until the sixteenth century BC, but work has so far been concentrated on the cities of the mid-third and early second millennia. Excavation of the latter has made a major contribution to knowledge of the architecture and art of that period, but of far greater importance are the unique discoveries in the earlier level.

Here was a major urban centre with central acropolis and lower town, perhaps covering some 56 ha, encircled by a defensive wall. Excavation has exposed part of an acropolis palace, including an

administrative block with archive rooms and magazines. The destruction of the building by fire preserved much of its contents: carved furniture, miniature sculpture, seals, decorative stone inlay, pottery and one of the largest collections of cuneiform tablets ever found. The great majority of these tablets are administrative and economic in content but there are also literary compositions, lexical texts, royal edicts and correspondence and treaties. Because of their number and the difficulties posed by the Eblaite language, it will be many years before their publication — entrusted to an international committee — is complete, but preliminary studies provide a foretaste of the rich harvest of information which will eventually be available on the population, economy, institutions, religion, literature and political history of the city.

Any reconstruction of the society and history of Ebla must at this stage be provisional. Matthiae's account, based on the textual evidence available when the 1977 Italian edition went to press, has to a certain extent been amplified and clarified by subsequent research, mainly in the field of linguistics. The population was predominantly but not exclusively Semitic and the closest connections of the Eblaite language are now considered to be with Akkadian, the speech of the Semitic element in the population of Sumer. A considerable amount of information is available on state and municipal administration but there remain many fundamental questions, answers to some of which may not be provided by the type of text found so far. For instance, was kingship hereditary or elective? What proportion of the population was in the service of the state, the temple or large land-owners and under what conditions?

Whether Ebla was the leading state of northern Syria and the centre of an extensive empire, as maintained by Matthiae, requires further investigation, but its conquests included Mari and it was in diplomatic contact with states as far east as the Tigris valley, notably Ashur with which it concluded a commercial treaty. Its far-reaching trading operations are documented by an archive dealing with the state-controlled export of woollen cloth. The destinations of the consignments are distributed over an area extending from Palestine to central Anatolia and from the Mediterranean to Ashur and Kish in northern Sumer. These names of towns and kingdoms provide much new information on political geography but although some are well known, such as Megiddo and Lachish, the majority cannot be located and there are numerous uncertain readings.

The civilization of Early Bronze Age Ebla was formed by the fusion of Syrian and Sumerian cultural traditions. The former are at present most evident in language, religion and architecture; the latter in the use of the cuneiform script, in

literature, art and certain administrative practices. The extent to which political and social institutions were influenced by those of Sumer is not yet clear. Until the lower levels of the site are investigated, the environmental and cultural factors which contributed to the rise of urban life at Ebla must remain a matter of speculation. However, archaic Sumerian elements in the political concepts and art of the palace period suggest that Sumer provided the initial stimulus, probably in the late fourth millennium when it had trading colonies in Syria.

It seems probable that the palace and its archive, which spans the reigns of five kings, was destroyed either by Sargon, founder of the Agade dynasty of Sumer, or by his grandson, Naram-Sin. According to one school of thought, the form of the script employed at Ebla requires the earlier dating. Matthiae prefers the later on the basis of certain artistic features.

The rediscovery of Ebla is of outstanding importance for the early history of civilization in the Near East. The texts and archaeological finds recovered from the palace have revealed the presence in northern Syria in the mid-third millennium of an established urban and literate Semitic society, as advanced as that of contemporary Sumer. The nature of the impact of Sumerian civilization on what was clearly a strong native cultural tradition can already be defined in considerable detail. The texts, when published, will illuminate the history not only of Ebla but also of the numerous states with which it had political and commercial contacts. The significance of the information obtained from Ebla cannot as yet be fully assessed but Matthiae indicates the areas in which it is to be sought. □

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The art of Ebla: wooden figure of a king from Palace G.

The appeal of archaeology

Gail Kennedy

The Cambridge Encyclopedia of Archaeology. Edited by Andrew Sherratt. Pp.495. (Cambridge University Press: 1980.) £18.50, \$35.

THE goal of this handsomely produced volume is to "summarize the present state of knowledge over the whole field of archaeological inquiry". While *The Cambridge Encyclopedia of Archaeology* does not quite achieve that somewhat quixotic goal, it does succeed to an impressive degree.

The overall value of the volume, however, rests as much with its clear presentation of the new directions taken by archaeologists since the 1960s, as with its summarization. In the past most books of this large-format genre have reflected

the earlier emphasis of archaeologists on the exquisitely formed artefact or imaginatively recreated structure; such books have relied more on lavish illustrations and less on informative text. While this volume is indeed well illustrated, the emphasis is on maps and schematic diagrams rather than artefacts, which here are pictured simply and in black and white. The maps — of physical geography, migration patterns, political domains and urban or village street plans — are among the most beautiful and informative in print.

While the maps and diagrams will undoubtedly set a publishing standard for the future, the text is no less attractive and informative. It clearly reflects the trend among archaeologists away from the antiquarian-collector attitudes of the past and

towards data synthesis, broad regional analyses and model building. It demonstrates clearly that archaeology today is problem-orientated rather than artefact-orientated. The problems now under examination by archaeologists often centre on the dynamics of interactions between man, his technology and the environment. Systems theory and feedback models provide valuable ways of examining such interactions, and indeed many of the sections in the *Encyclopedia* are structured either implicitly or explicitly around these conceptual frameworks.

A systems approach becomes a particularly useful tool in archaeology when analysing the emergence of entirely new levels of organization. No longer are such new levels viewed by archaeologists as periods of abrupt revolutionary technological or behavioural change, but instead are seen as periods of adjustment and readjustment to changing configurations of resources and knowledge. The origins of agriculture form one of the more intriguing applications of systems theory. At the end of the last glacial, environmental changes apparently provided both the opportunity and the necessity for the increasingly specialized exploitation of food resources. What is well demonstrated in the chapters on the origins of agriculture in the Near East, Africa and the Far East is that this new and unique strategy for human survival occurred, apparently independently, in several areas. Thus, in each of these major regions, and in at least one centre in the New World, human populations responded to the changing post-glacial world in a recurring pattern of increased utilization of a small number of wild foods. It was this emerging dependency on wild foods which led to their ultimate control and domestication. And it was this control over local food resources that paved the way for an increasingly sedentary way of life.

The variety of subjects covered by the book is indeed encyclopaedic. While most of the chapters consist of regional analyses of important phases in human history — the origin and development of agriculture, cities and empires, for example — other relevant topics such as early human evolution and dating techniques have not been neglected. The geographical scope, however, is somewhat uneven. Of a total of 64 chapters, only seven (eight if one includes Oceania) are devoted to the archaeological history of the New World. While it may be conceded that the Old World was long the central focus of human development, surely the entire Western Hemisphere merits more discussion than these few rather perfunctory chapters. Moreover, certain major problems in New World prehistory, such as the probable timing and route of human entry, have not even been mentioned.

In the final analysis, the faults of *The Cambridge Encyclopedia of Archaeology* are few. The short, well-illustrated

chapters are suited for both browsing and more directed reading, while their content will inform all but the specialist. Although price is a drawback, this would be an extremely useful text for broad survey courses in archaeology. The consistent emphasis on method, theory and recent

research, the bibliography and broad geographical and temporal scope all combine to make this a volume with wide appeal. □

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Cancer: how much of a business?

D.G. Harnden

The Cancer Syndrome. By Ralph W. Moss. Pp.347. (Grove Press: 1980.) \$12.95, US only.

It is usually assumed that those involved in cancer research are motivated by a desire to rid the world of the disease. While this may be partly true, intellectual curiosity and concern for individual patients are often the most potent driving forces. Ralph Moss, however, tells us something different. Cancer research in the USA is, he says, largely manipulated by big business in the hope of financial gain; manipulated by those who believe that a cancer cure will make a fortune for the holder of the patent and by those who fear that preventive measures will involve cleaning up a profitably polluted environment. The medical profession too, he suggests, are part of this conspiracy, favouring treatments which ensure a handsome profit.

It would be easy to dismiss Moss's book as inaccurate in detail and outrageously biased, but to do so would be to fail to acknowledge that some of the criticisms that he makes seem well aimed and that the issues he raises are of considerable importance. Unfortunately, he does not spell out or consider in any constructive way the main issue that he raises, namely "What is the proper relationship between the fundamental discoveries of biological science and the industry that can make these discoveries available to the general public?"

There are two central allegations around which the book is built. First, that orthodox treatment is unsuccessful and that the cancer establishment in the USA will take any steps to ensure that new developments which are not patentable are stifled at birth or as soon thereafter as possible. Second, that little emphasis has been placed on prevention because it would be more profitable to find a patentable cure and because prevention might involve fundamental and expensive alterations in industrial practices.

Is there any truth in either of them? For the commonest cancers it is true that the results of conventional treatment are not good. In breast cancer the five-year survival rate is approximately 50% (and, as Moss reminds us, five-year survival is not cure), while for lung it is a disastrous 5%. Even worse, neither figure is improving. When we say that improvements have

occurred over the past few years it is essentially in cancers that are uncommon, such as Hodgkin's disease and in the childhood neoplasms such as Wilm's tumour. But many cancer patients are cured and many more are given a greatly improved quality of life, so there is, at least, some over-statement. However, when Moss points to over-optimistic propaganda about cures it is hard to disagree with him — we have a long way to go. He therefore suggests that we turn to unorthodox methods such as laetrile, Coley's toxin, hydrazine sulphate and vitamin C, and says that information that such methods are already successful has been deliberately suppressed. In a vitriolic attack on the Memorial Sloan Kettering Cancer Centre, the American Cancer Society and the National Institutes of Health, he accuses these institutions and specific individuals of blocking grant awards for research in these areas and of granting awards to others for their help in this process.

As a science writer sacked from the Memorial Sloan Kettering for misrepresenting the work of the Institution, Moss can hardly be without bias — but he is well informed. He shows that the governing bodies of the Memorial Sloan Kettering Cancer Centre and the American Cancer Society have a large representation of those whose business connections could lead to a conflict of interest. Obviously there are altruistic reasons why industrialists and financiers would wish to serve on the board of a cancer centre, but there could be less worthy reasons. Although overt attempts to influence scientific policy would obviously be resisted by the scientific staff, the possibility of indirect influences, especially by those who donate very large sums of money to the institutions, must be a matter for concern. Moss also points to the form of contract between the Memorial Sloan Kettering Cancer Centre and the chemical companies which seems to grant all the advantages to the companies. This is not an easy matter, and the link between industry and the scientist often poses a dilemma. Anyone in cancer research who has a connection with industry is liable to be accused of having compromised his scientific integrity. However, Moss is more concerned with undermining the present structure than with suggesting improvements and the important questions are left unasked.

It really does seem hard to believe that successful unorthodox treatments are suppressed because they are not patentable. If they were good then they would have been adopted in countries other than the USA where the allegations of corruption levelled by Moss do not apply. Moreover, Moss mentions, but gives scant attention to the need to protect the public from unscrupulous frauds. There are too many documented cases to ignore the fact that National Institutes of Health, the American Cancer Society and similar bodies have a duty not only to promote research, but also to protect the public from quacks. So the first charge is not entirely proven; nonetheless, Moss's book leaves an uncomfortable feeling that all is not well.

When he turns to cancer prevention (or the lack of it) he is on firmer ground. There is plenty of evidence that in the past, and also at present, some parts of industry have callously ignored the welfare of their workers. Moss revels in the horrors of asbestos and mesothelioma. These facts have been well documented elsewhere, however, and are no longer the main issue. He is quite wrong in saying that research into preventive methods has been ignored;

this only reveals his limited horizons. There is at present a great deal of activity in basic research laboratories and in industrial laboratories to find ways of preventing the widespread use of hazardous chemicals. Again, this needs collaboration between industry and basic research, but the relationship is not always an easy one. Any scientist who helps a company to sort out a problem is likely to be branded a consultant — and therefore suspect — by people such as Moss. This should not be so — the expertise in the universities and research institutes *should* be available to industry. On the other hand, it does cause concern that one distinguished scientist and government adviser should also be found to be a consultant for six large corporations and two manufacturers' associations.

The book is well written and easy to read. In an era in which monoclonal antibodies and the production of specific polypeptides by genetic manipulation are likely to become big business, it raises issues that have to be faced. The manner in which the issues are raised, however, leaves a rather nasty taste in the mouth. □

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State of the art in nutrition

J.W.T. Dickerson

Human Nutrition—A Comprehensive Treatise. General editors R. B. Alfin-Slater and D. Kritchevsky. (Plenum: 1979/1980). Vol. 1. *Nutrition: Pre- and Postnatal Development* (edited by M. Winick), pp.495; £24.89, \$39.50. Vol. 2. *Nutrition and Growth* (edited by D.B. Jelliffe and E.F.P. Jelliffe), pp.450; £23.63, \$37.50. Vol. 3A. *Nutrition and the Adult: Macronutrients*, pp.290; £15.75, \$25. Vol. 3B. *Nutrition and the Adult: Micronutrients*, pp.424; £24.89, \$39.50. (Both edited by R.B. Alfin-Slater and D. Kritchevsky.) Vol. 4. *Nutrition: Metabolic and Clinical Applications* (edited by R.E. Hodges), pp.478; £23.63, \$37.50.

THIS large work has grown out of an idea "to provide the research investigator and the advanced graduate student with an up-to-date report on the state of the art". Originally intended as one volume, the treatise now has four volumes and one (Vol.3) has two parts.

Volume 1 deals with the role of nutrition in pre- and postnatal development, and starts with a discussion of nutrition and the metabolic development of mammals. Metabolic status at various stages of development is closely related to the quality and quantity of the nutrients consumed. The author (Hahn) suggests that the old idea that nutrients act directly on most cells must be discarded and

replaced by a concept that, mostly, nutrients have immediate and long-term effects by acting on selected endocrine cells, which then release their hormone to act on target cells. It is this combined effect which controls the development of enzyme systems, cells and tissues.

The development of the brain is important in controlling the ability of the organism to respond to its environment and malnutrition may, because of the time-scale over which the brain develops, have permanent deleterious effects upon it. The importance of this subject is reflected in several of the following chapters.

Nutrition and pregnancy is largely discussed from the viewpoint of the effects of disturbances in maternal nutrition on the growth and development of the foetus. The effects of nutrient excesses and of interactions of drugs with nutrients are briefly mentioned. This leads logically to a discussion of breast feeding by Jelliffe and Jelliffe who make the point that the matters that need emphasis are the same the world over.

The contribution to the interactions of nutrition and infection includes a discussion of the problem of the septic patient. In the chapter on the relationship of nutrition to dental development and disease the need is emphasized for more studies to explore the mechanisms and consequences of nutrient deficiencies to oral health. The recognition that

atherosclerosis may be a paediatric problem is dealt with. Although this is a prudent approach it is emphasized that proof is at present lacking. A brief chapter is devoted to inborn errors — principles and not details. The final chapter discusses the management of chronic diarrhoea in children.

The second volume, concerned with nutrition and growth, draws attention to the diffuse nature of the subject, the value of having different perspectives, and the fact that there are few "absolute" answers to the various problems such as standards for growth and dietary allowances.

The first chapter considers the problem of nutrient needs. In the absence of proper experiment, the tendency is to consider present intake as "ideal requirements". In the next chapter the complex interrelationships between genetic constitution and nutrition are discussed. The influence of non-dietary factors is dealt with, as also is the problem of metabolic anomalies.

Part II is concerned with the ages of man and is introduced by a chapter on maternofetal nutrition which presents results of the 1969 longitudinal INCAP study. This leads logically to a consideration of the nutrition of the full-term and premature baby. The need for further work on the problems of the latter is emphasized. Four chapters are then devoted to the young child and discuss the normal and failure-to-thrive child, protein-energy malnutrition and obesity respectively. The adolescent, rapidly changing organism and the adult, stabilized situation between development and senescence are then discussed. Part III contains nine contributions which deal with aspects of growth monitoring and nutritional assessment and surveillance, and contains much practical information on different methods and useful tables of reference data.

Volume 3A starts with a discussion of nutrient requirements — what they are and the bases of recommendation — leading on to contributions concerned with energy requirements, the suppliers of energy and their interrelationships, the problem of energy exchange and the partition of food energy. The remaining four chapters deal with nutrients with special functions — proteins and amino acids, essential fatty acids, cholesterol and dietary fibre.

Volume 3B is introduced with a chapter on vitamins, mainly those of the B-group, as co-enzymes. There are five chapters on individual vitamins and one on iron-haemoglobin. The chapter entitled "Trace Elements" starts with a somewhat scant treatment of calcium, phosphorus and magnesium. There are useful discussions of drug-nutrient interrelationships and the effects of oral contraceptives on nutrient requirements. The final chapter on nutrition of the elderly has very much a North American bias.

Volume 4 is concerned with the metabolic and clinical application of nutrition.

The first three chapters discuss the relationship of nutrition to disorders of the haematopoietic, nervous and musculoskeletal systems respectively. These chapters are not exhaustive and are not concerned with therapeutic aspects. The effects of essential nutrients on the gastrointestinal tract and the effects of diseases of the tract on the absorption and utilization of nutrients are dealt with, as also are the nutritional abnormalities occurring in liver disease. Here again there is no discussion of the possible role of nutrition in treatment. This is in contrast to the presentation on cardiac failure which is much concerned with therapeutic aspects and contains a useful table of drug-nutrient interactions of importance in congestive heart failure.

Discussion of the relationship of diet and nutrition to cancer is mainly concerned with their possible involvement in the aetiology of oncological disease, with little mention of the effects of the disease on the nutrition of the patient.

The ageing-nutrition-health triad is discussed by Watkins who points out that education is the prime catalyst for inducing change. The chapter on the endocrine system is concerned with diabetes, vitamin D, and parathyroid and thyroid disorders. Discussion of megavitamins and food fads is largely taken up with doubts about Pauling's well-known views. It is, perhaps, unfortunate that in a text of this sort some consideration is not given to the possibility that larger amounts of vitamins than the currently recommended allowances may have beneficial effects which are difficult to measure and therefore often dismissed as anecdotal.

There is a useful and well-referenced chapter on the effects of ethanol. Nutritional aspects of infectious diseases

are discussed and it is pointed out that nutritional supportive therapy should be employed to prevent or minimize the depletion of body stores during an infection, and to replace lost nutrients as expeditiously as possible during convalescence. Obesity is the most common nutritional disease in Western society. Assessment, risks and treatment of this poorly understood condition are considered. As a consequence of our poor understanding successful treatment is often elusive, and the demand for treatment has led to a multiplication of fad diets, examples of which are given. The final chapter contains a discussion of the interrelationships of nutrition and the kidney. Effects on kidney function and nutritional disturbances in the nephrotic syndrome, hypertension and renal failure are dealt with, as also are the principles of nutritional therapy.

These volumes are a useful addition to the textbooks available on human nutrition. They are not exhaustive, either in respect of subjects covered or the depth to which each subject is discussed, but the material is well presented and well referenced throughout. Moreover, the books have been produced to a high standard and are a pleasure to read. In spite of their inevitably high price, teachers of nutrition at degree level may well consider it worthwhile acquiring one or more of them. They can be said to have achieved their aim and to present in reasonable compass the present state of the art in a dynamic subject. □

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subject, of course, to the disabilities consequent upon their pre-operative brain damage.

Here we also had a neurosurgical preparation in which, with appropriate techniques that were lacking in the 1940s, one could investigate the cognitive capacities of the left and right hemispheres isolated from each other except through their brain stem connections. The preparation enabled workers to confirm, extend and fine the deductions that had previously been drawn from the effects of lateralized injury, namely, that the left and right hemispheres (in the majority of the population) are indeed primarily implicated in the exercise of linguistic and visuo-spatial skills, respectively. But because in the commissurotomy patient the left hemisphere has little knowledge of what the right hemisphere is doing (and vice-versa), the enticement of talking about these people as if they had two minds within a single body (brain? person? soul?) proved irresistible (and not only to popularizers). The lure of thinking about the patients in this way is, of course, much more exciting than patiently trying to comprehend the what, how and why of functional localization.

But worse was to come. The disconnected right hemisphere, conspicuously deficient in syntax and verbal reasoning, can yet support dreams, emotions, and a high level of non-verbal memory and intelligence. All that remained was to deify the distinction between the cerebral hemispheres: the left brain became the seat of a cold, calculating, logical and talkative mind, whilst the right brain sustained a warm, intuitive, emotional and artistic mind. In an era in which attitudes towards science are often ambivalent, what could be more attractive than to have science and surgery discover the reality, nay the material substrate even, of intuition, creativity and pure feeling.

Modern times are truly an ideal medium in which to culture the hundreds of articles and books that have attempted to disseminate "the right brain revolution" that Blakeslee describes. Yet there is a sense in which any sociological analysis provides too easy a let-out. Blaming the *Zeitgeist* never takes us very far. The real vacuum that such books attempt to fill arises from the failure of neuroscientists themselves to provide any significant theoretical account of functional localization. The evidence — from anatomy and pathology, and from recordings of the electrical and chemical activity of the normal intact brain — now overwhelmingly supports the notion that distinct cerebral regions are differentially involved in the exercise of higher cognitive functions. How and why this is the case we do not know. It could, however, be an interesting problem for someone to work on. □

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Abdication of reason

John C. Marshall

The Right Brain: A New Understanding of the Unconscious Mind and its Creative Powers. By T. R. Blakeslee. Pp.275. (Papermac/Doubleday: 1980.) Hardback £10, \$10.95; paperback £2.95.

THIS is another "popular" book on how to unlock the emotional and creative power of the right cerebral hemisphere. The volume recounts some of the evidence, from both normal and brain-injured people, that has led physicians and clinical psychologists to believe that considerable specialization of function characterizes different areas of the human brain. Blakeslee concentrates on inter- rather than intra-hemispheric localization and leaps somewhat wildly from datum to conclusion. For any reviewer who wants to dip into his repertoire of sarcasm, the volume will provide more than adequate stimulus — why is there no woman Beethoven, the author asks, and answers that the cerebral

hemispheres of women are functionally less differentiated than those of men. It is tempting to regard Blakeslee's offering as beyond satire and plunge immediately into instant sociology. Why do such books exist? What need do they satisfy?

The "right brain revolution" that Blakeslee and so many others have attempted to explain to a lay audience had its genesis in 1962. Two Los Angeles neurosurgeons, Philip Vogel and Joseph Bogen, revived and refined a surgical procedure for the control of pharmacologically intractable epilepsy. The operation involved sectioning the corpus callosum and the anterior and hippocampal commissures — the main fibre tracts that interconnect the two cerebral hemispheres at the cortical level. There can be little doubt that both the original and subsequent series of commissurotomy operations have been a success; patients whose intellectual and social activity had been severely compromised by generalized convulsions have been able to return to an essentially normal life, although still

REVIEW ARTICLE

Carbonic metamorphism, granulites and crustal growth

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Stabilization of early crust against melting by high radioactivity and against resorption into the mantle by fast convective overturn requires that water and heat producers were flushed upwards within 50 Myr of accretion. Creation of a refractory base of granulite by metamorphism associated with CO₂ vapour explains CO₂-rich fluid inclusions in ancient high-grade rocks, minor-element depletions and local phenomena of arrested development of charnockite in Precambrian terrains. The hot-spot and plate-tectonic models of Precambrian crustal evolution lead to different schemes for CO₂ delivery to continental roots. New tectonic concepts may be needed to explain carbonic metamorphism and other features of early crustal evolution.

THE continental crust consists of a heterogeneous assemblage of rocks whose crystallization ages fall into clusters dating back¹ 3,800 Myr. If earlier crust existed, it was presumably destroyed by resorption into the mantle or by meteorite impacts, by analogy with the Moon². Radiogenic heat production would have halved during the period³ 4,500 to 3,000 Myr ago, but even by 3,000 Myr the latest estimate of total heat production of the Earth⁴ implies an average volcanic activity for the Earth's surface similar to that of Iceland at present⁵. The important problem is thus how the continental crust became stabilized in the Archaean era against melting at its roots, and against resorption into a rapidly convecting mantle.

The well exposed Archaean terrain of south-west Greenland contains areas of tonalitic gneisses with two discrete ages (Amitsoq, 3,650 to 3,700 Myr; Nûk, 2,800 to 3,000 Myr).⁶ Other terrains support the concept of major episodes of crustal accretion from partial melting of mantle, and the similarity of initial isotope ratios to model values for mantle evolution implies little contamination by earlier crust⁷.

Ancient terrains are generally metamorphosed into the amphibolite and granulite grades. The mineral chemistry of the granulites demonstrates reaction over a pressure range⁸ ~7–12 kbar (0.7–1.2 GPa), which corresponds to a depth range of ~25–40 km before uplift in response to erosion and tectonic forces⁹. Granulite rocks contain much less H₂O than lower-grade rocks with similar major-element chemistry: anhydrous pyroxene minerals are prominent in granulites whereas the hydroxylated minerals mica, amphibole and epidote are the mafic equivalents in rocks of amphibolite facies. Charnockite, a pyroxene-bearing rock of granitic composition, is a conspicuous type of granulite which dominates some granulite terrains (for example, southern India). Some charnockites have igneous precursors^{10,11}, but some have been attributed to metamorphism of layered sediments¹² and anatexis mobilization of graywackes¹³.

Many granulites have lower contents of large-ion lithophile elements (for example, U, K, Th, Rb) and heavy rare earths than younger crustal rocks with similar major-element chemistry^{14,15}. Heat-flow and heat-balance¹⁶ calculations demonstrate that the lower part of the continental crust is strongly depleted in radioactive elements with respect to upper crustal rocks, and show that widespread crustal melting by intrinsic heat produc-

tion would have taken place in the Archaean unless the radioactivity was strongly concentrated in the uppermost part of the crust by some transport mechanism within 50–100 Myr after an accretion episode³. Hence granulites are the obvious candidates for deep continental interiors, and granulitization, either by igneous or metamorphic processes, or both, deserves detailed study.

A unique feature of many granulites is CO₂-rich fluid inclusions in minerals, in contrast to H₂O-rich inclusions characteristic of lower-grade metamorphic rocks^{17,18}. Hence carbonic volatiles may be important in granulite metamorphism and continental stabilization^{9,15,19,20}. For carbonic metamorphism to be applicable to entire continental bases, a large, possibly subcrustal, source of CO₂ would be needed. Carbonate-bearing peridotite is stable in the mantle to higher temperature than mica-peridotite²¹, and is a possible source of CO₂. Interrelations among granulites, crustal growth, carbonic metamorphism and mantle storage of CO₂ are now examined with reference to simple tectonic models currently being discussed for evolution of Precambrian crust.

Origin of granulites

It has been suggested that granulite terrains in general are the residues of crust depleted in H₂O and lithophile elements by partial melting (anatexis), with removal of the melt phase to shallow depths²². However, there is much evidence against this hypothesis. K-rich granites and higher-level amphibolites are not complementary in either major or minor elements to many granulites^{9,15}. Indeed, some granulites, such as the Madras charnockites²³ with granitic chemistry and high Fe/Mg, would themselves qualify as the out-melted fraction. In some migmatite areas, both out-melted and residual fractions are in the granulite facies²⁴. Tonalitic gneisses have similar Ba/Sr in both amphibolite and granulite grades; the latter could not be residues from closed-system melting of the former because of greater preference of Ba over Sr for a melt fraction¹⁵. It has been shown that outmelting did not occur extensively during the 2,700 Myr granulite metamorphism of the Scourian terrain of the Scottish Highlands, the key evidence being preservation of the 2,900 Myr Sm–Nd age²⁵. Although granulites cannot in general be anatexis residues, some pyroxene gneisses might be

residual fractions of mantle or deep-crustal melts^{26,13}. The pronounced depletion of heavy rare-earth elements of many pyroxene gneisses may require a two-stage formation: original accretion of a basaltic pile and remelting of the basalt to produce tonalite at depths great enough to stabilize garnet in the residue¹⁵.

Granulite terrains contain a wide variety of bulk compositions matching the metamorphosed igneous and sedimentary components of lower-grade terrains. In Karnataka, India, the metamorphic facies changes southerly from greenschist to granulite²⁷. Marbles, basic rocks, pelites, migmatites, Fe-rich quartzites and dominant tonalitic gneisses occur over hundreds of kilometres, and granulite metamorphism, which has affected all of these lithologies, is not obviously associated with partial melting and complementary residues. A similar situation exists in south-west Greenland⁹.

Although many or most granulites have not undergone extensive partial melting, a mineralizing pore fluid is needed to explain the coarse K-feldspar in pegmatoidal charnockites from Enderby Land²⁸ and Pallavaram, Madras²³. Kinetic calculations (see ref. 29) show that growth of large garnets at metamorphic temperatures requires a flux. A pervasive fluid would help to transport minor elements¹⁵. The discovery of dense, CO₂-rich fluid inclusions in minerals of granulites¹⁸, and the intimate connection between charnockite and CO₂-rich inclusions over broad terrains, points strongly to the role of CO₂ in the metamorphism. In the Bamble terrain, southern Norway, fluid inclusions change from aqueous in amphibolite facies to carbonic in granulite¹⁷. The Kleivan pluton, south-west Norway, grades from normal granite with aqueous inclusions to charnockite with carbonic inclusions^{30,31} over 5 km. In the zone of regional transition from amphibolite to granulite in Karnataka, patches of charnockite are locally developed in amphibolitic gneiss²⁷. Irregular diffuse stringers of dark-brown charnockite obliterate the pronounced migmatitic banding of gneisses over a scale of 1 cm to 1 m. Amphibole and biotite of amphibolite give way to pyroxenes in patches of charnockite with no textural evidence of melting²⁰. Temperatures could not have risen significantly over 1 cm to produce dehydration. Influx of CO₂ along shears was invoked to explain the dehydration. Similar patchy distribution of charnockite occurs in south-west Greenland⁹, south-west Sweden¹³ and western Australia³². The fluid in cordierite from Finnish granulites has CO₂ mole fractions³³ ranging from 0.35 to 0.85; cordierites from some rocks in the amphibolite facies have much higher H₂O/CO₂ than cordierites from Norwegian granulites³⁴; and cordierites from shallow pegmatites contain no CO₂ in contrast to abundance in cordierites from granulites³⁵.

This evidence for abundant CO₂ complements evidence from experimental and theoretical phase-equilibrium studies that granulite-forming fluids must have low P_{H_2O} . Mineralogical geothermobarometry of granulites consistently yields temperatures of 700–900 °C and pressures^{23,36} of 7–12 kbar. However, many rock types yield granitic liquids at 650–700 °C and P_{H_2O} of a few kbar (ref. 37). In particular, the definitive charnockitic assemblage K-feldspar + orthopyroxene transforms to biotite + quartz or partially melted assemblages at water pressures above 0.7 kbar, regardless of the temperature³⁸. To avoid melting, the water fractions of metamorphic fluids must be low, such as the 0.1–0.3 estimated for the amphibolite-to-granulite transition in the Archaean terrain of south-west Greenland⁹.

It must be emphasized that experimental work and geothermobarometry indicate that simple metamorphic dehydration reactions are not sufficient to account for the dryness and minor element depletion of granulites. Some overwhelming pore fluid diluent is called for, and the fluid inclusion evidence implicates CO₂.

Amount and source of carbonic fluids

The upper limit of $P_{H_2O} = 0.3P_{total}$ for granulites from south-west Greenland allows rough estimation of the amount of CO₂ required for conversion of amphibolite to granulite over a

20-km thick layer of crust. A continuous flushing action is needed because H₂O from the breakdown of hydrous minerals would otherwise dilute the CO₂. For a conservative estimate of 1 wt% of H₂O in amphibolitic gneisses and an ideal gas law, about 8 wt% CO₂ is needed ($44/18 \times 0.7/0.3 \times 1$ wt%), or roughly 0.3 rock volume at average temperature and pressure. This much CO₂ is ultimately necessary to convert an amphibolitic crustal layer to granulite, and the supply may possibly be maintained over the duration of a metamorphic episode, say tens of Myr. The actual amount of CO₂ in the rocks at any instant may be very small, in the form of grain-boundary films.

Thin marbles and calc-silicates occur in greenstone piles and as metamorphic relics in Archaean high-grade terrains³⁹. Calc-silicate rocks, possibly representing former limestones, are conspicuous locally in some terrains but are usually subordinate to associated charnockites and other granulites⁹. Although the graphite contained in many Precambrian metasediments³⁹ might react with H₂O to produce CO₂ at high temperature and pressure, the mole fraction of CO₂ produced by reaction in a closed system is below 0.7 for a large range of T and P (ref. 40). Osmotic escape of H₂, or fluid immiscibility⁴¹, might cause CO₂ enrichment.

Some authors have dismissed crustal sources of CO₂ as inadequate to produce the kind and degree of metamorphism observed^{9,20}. However, it is very difficult to estimate the original CO₂ content of a highly metamorphosed section. Extensive evaporite sequences rich in carbonate and organic carbon have been recognized recently in the Archaean of Brazil⁴², and stratigraphy of this sort may have been more abundant than generally recognized. We emphasize here mantle outgassing as a more feasible CO₂ source^{9,19,43,44}, while recognizing the inherent difficulty of assaying possible crustal contributions.

The present-day mantle contains substantial CO₂ in spite of extensive partial melting. Hawaiian volcanoes emit CO₂-rich gases⁴⁵. Mid-ocean ridge basalts contain CO₂-bearing vesicles⁴⁶ and xenoliths of mantle peridotites contain fluid inclusions of nearly pure CO₂ (ref. 47). A high CO₂ activity is important for generation of alkali basalts and carbonatites^{48–50}. Depending on the P - T regime, the CO₂-bearing phase in equilibrium with olivine and pyroxene of the mantle is either a carbonate (dolomite or magnesite), a CO₂-rich melt, or a free vapour^{21,51,52}. To provide 0.3 rock volume of CO₂ for 20 km of crust, 0.04 rock volume would be required from an assumed 150 km of uppermost mantle; this corresponds to ~1–2 wt% of carbonate minerals or interstitial carbonate-rich melt.

Mantle carbon, as represented by diamond and carbonatites, has a smaller amount of ¹³C ($\delta^{13}C \cong -6\%$ relative to the commonly used standard) than limestone, which averages about +20%. Carbon from the CO₂-rich fluid inclusions of Bamble granulites is near the mantle value, which was used as evidence of a 'primary' carbonic fluid from the upper mantle⁵³. However, graphite of biogenic origin is also very light⁴², and it is not clear how much this may have influenced the granulite fluid inclusion carbon. Isotopically light carbon is a necessary, but not sufficient, criterion of a subcrustal source.

If the whole Earth went through a vapourization stage at the end of accretion⁵⁴, it is not obvious how to explain the presence of CO₂ and other volatiles (for example, ³He) in the Earth's mantle⁵⁵. Late accretion of cool volatile-rich material on to an Earth that had been cooled by intense volcanic activity during accretion⁴ is more plausible. If the primitive mantle was effectively degassed during an early period of high temperature, some form of subduction is needed to carbonate the mantle. Recent experimental data suggest that some pelagic limestone, perhaps inorganically precipitated, might escape dissociation and melting during subduction into the mantle⁵⁶. Carbonate-bearing peridotite is stable to higher temperature and should tend to resist melting better than mica-bearing peridotite above 26 kbar (ref. 21), during convective overturn of the mantle. Although there is no compelling evidence for plate-tectonic subduction in the early Archaean, assimilation of carbonate-bearing sediments into the crust may have occurred during

destruction of crust⁴ before 3,900 Myr BP. If the Earth's mantle contained elemental carbon at the end of accretion, oxidation to CO₂ might have occurred during transportation to the surface by convective overturning, or by disproportionation of ferrous iron into ferric iron and iron metal at high pressure⁵⁷.

Phase-equilibrium constraints on carbonic metamorphism

Some experimental phase-equilibria⁵⁸ would allow partial remelting of a basaltic lower crust to yield tonalitic liquid and a garnet-bearing residue. The latter would provide a sink to explain heavy rare-earth depletion in granulite (that is, anhydrous) conditions. A two-pyroxene granulite of basaltic composition begins to melt to garnet + clinopyroxene + liquid at ~1,190 °C for 11 kbar and 1,230 °C for 15 kbar (ref. 58). In the subsolidus region, olivine and orthopyroxene are progressively eliminated with increasing pressure, and garnet becomes stable at ~10 kbar. A late Archaean geotherm³ would allow dry basalt to melt to a garnet-bearing residue and a tonalitic liquid at ~12.5 kbar and 1,200 °C. The experimental melting relations place an effective limit of ~40 km on the thickness of the Archaean crust with this geotherm, which passes near a *P-T* estimate for Madras granulites²³. Formation of carbonate-bearing scapolite in basaltic to intermediate compositions places limits on the conditions in which CO₂ may stream through the lower crust. Although calcic CO₂-scapolite is stable by itself to very high temperatures at elevated pressures, the retention of CO₂ by basalt is limited by the reaction:



The *P-T* location of this reaction is not yet known, but a moderately large geothermal gradient (see, for example, ref. 3) would probably pass through the free-CO₂ field (right-hand side of the above reaction) for about the lower half of the crust. Details depend on the Na/Ca ratio of the plagioclase and the CO₂/SO₄ ratio of the scapolite, and much further experimentation is needed.

A basaltic liquid rising from the mantle would release CO₂ during ascent, either because of greatly decreased solubility below 20 kbar (ref. 48), or because of crystallization. At 10 kbar, basaltic magma saturated in CO₂ and H₂O releases a vapour with CO₂ mole fraction⁵⁹ near 0.9, and such a vapour would be rich enough in CO₂ to purge overlying crust until it became too diluted in captured H₂O.

Another possibility is transport of CO₂ during crustal accretion by the dissolved volatile complement of primary tonalitic liquids generated directly by mantle melting⁹ leaving a garnet-bearing residue, perhaps in a subduction zone. Evaluation of this and related possibilities requires discussion of tectonic mechanisms of Archaean crustal accretion.

Tectonics of carbonic metamorphism

Because many granulites should still be buried and because many must have been destroyed by retrograde metamorphism, there is considerable doubt about the rate of generation of granulites throughout geological time. The simplest tectonic model involves continuous outgassing of CO₂ from the mantle into the lower crust. By analogy with the evidence for generation of crust¹, the supply of CO₂ would have been episodic. Subduction of carbonate sediments and their assimilation into peridotite might replenish the mantle reservoir, and convective overturning would take newly carbonated peridotite under a continent where CO₂ could be released to cause carbonic metamorphism. However, a comprehensive model should consider the problem of the great concentration of granulites in the age range 3,000–2,500 Myr and show the relationship of these granulites to other components of the Archaean crust.

There is no agreement on the tectonic relationships between low-grade greenstone belts and high-grade regions of the

Archaean era, and simple analogies based on modern plate-tectonic^{60,61} and hot-spot^{62,63} models may be misleading because of possible change of convective style and melting processes in the mantle as heat flow declined. Hot-spot models are inspired by extrusion of large volumes of basalt at Hawaii and Iceland where generation of proto-continental nuclei may be occurring. Plate-tectonic models draw support from (1) calc-alkaline nature of island-arc volcanic rocks and probable andesitic composition of mean continental crust⁶⁴; and (2) analogies between ancient rocks in granulite-gneiss Archaean belts and deeply eroded Cordilleran batholithic belts⁶⁵. A linear sequence of ridge, trench and subducted slab is probably incompatible with the high heat flow⁴ and unstable continental nuclei of early Archaean times. Perhaps numerous plume-like cells with radial rather than lateral spreading^{4,63,66} partly coalesced into short ridges as the Earth cooled. It seems certain that a tectonic model for development of granulites in high-grade regions will not prove fully satisfactory until the relationship to greenstone belts is explained. However, the tectonics of ancient carbonic metamorphism will be discussed with reference to the contrasting hot-spot and plate-tectonic models to focus attention on the problems of CO₂ delivery to the lower crust.

Hot-spot model

Basaltic magma from a rising mantle plume or diapir may escape to form a massive intrusion⁶³ under existing continental crust (Fig. 1a). Water is retained by amphibole in crystallizing basalt, and CO₂ escapes to flush out water from overlying crustal rocks¹⁸ to produce a granulite front. On cooling, an underplated basaltic pile turns into amphibole-bearing eclogite, garnet granulite, or garnet amphibolite. Underplated crust becomes distended, as perhaps in the present western US, and deep, block-faulted grabens are filled with basic lavas and detritus to become greenstone belts or cratonic supracrustal troughs. Note that the apparent trough-like nature of greenstone belts may actually be due to post-deposition tectonics⁶⁷. As the mantle

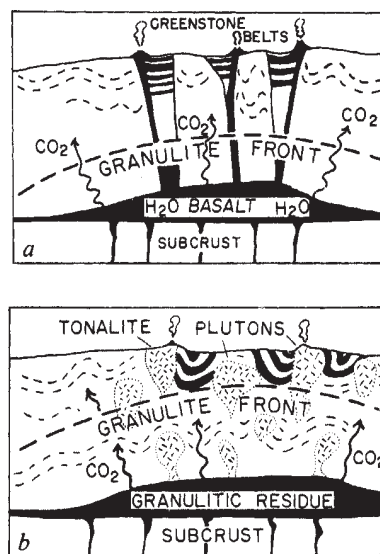


Fig. 1 Hot-spot model of crustal growth and granulite metamorphism. *a*, Basaltic liquid from a mantle diapir (not shown) underplates existing crust, and crystallizing amphibole retains H₂O. Doming of the crust results in massive grabens filled with volcanic and sedimentary rocks which become metamorphosed into greenstone basins (GB). A granulite front develops from carbonic metamorphism caused by CO₂ released either directly from the mantle or from crystallizing basalt. *b*, Steepening of the geotherm causes remelting of deep-seated rocks to yield a garnet-rich residue and uprising magmas. Resulting tonalite plutons rise through the crust causing isoclinal folding of greenstone basins. Further CO₂ streaming causes rise of a granulite front.

plume continues to rise, geothermal gradients steepen. The basaltic continental roots undergo partial melting to yield magmas of intermediate composition. These rise diapirically as tonalitic plutons which engulf the greenstone belts⁶⁶ (Fig. 1b). Escape of tonalitic magma leaves behind a mafic to ultramafic residue. Basaltic magma continues to escape from the mantle bringing further H₂O and CO₂. The key to this model is escape of CO₂ as a vapour phase at a pressure near 20 kbar while a secondary amount of H₂O is either trapped in hornblende in the deep crustal residue or transported upwards in a tonalitic liquid. Whereas H₂O may be transported to the surface in an under-saturated tonalite melt without significant reaction with crustal rocks, CO₂ vapour may diffuse upwards flushing water in front of it until either the H₂O/CO₂ ratio of the vapour becomes too high to remove further H₂O or the stability field of scapolite is reached.

The geochemistry of magma generation in rising mantle diapirs is not fully understood at present, and the possibility of generating intermediate calc-alkaline liquids in the presence of H₂O and CO₂ components directly by partial melting of the mantle under a hot spot must be retained as an alternative. CO₂ in the mantle might be expelled during partial melting or at least partially dissolved in the tonalitic liquid. Subsequent freezing of this liquid in the crust could release CO₂ for metamorphism.

Factors in favour of a hot-spot model are:

- (1) Field mapping and mineralogical geothermobarometry of post-Archaeon 'hot-spots' in continental settings: Adirondack Highlands⁶⁹, Wilmington Complex, Delaware⁷⁰, Naxos thermal dome⁷¹ and Massif Central, France⁷². Particularly indicative of a mantle origin for CO₂ is the low ¹³C of fluid inclusions from Naxos, in spite of abundance of local limestones. ¹³C-poor CO₂ of present-day carbonic acid springs in tectonic regions is attributed to a mantle origin⁷³.
- (2) Continental underplating provides a heat source for high-grade metamorphism of the lower crust. For Naxos⁷¹, a heavy CO₂ influx of 0.06–0.8 rock volume was estimated to provide enough heat to raise the regional blueschist terrain to migmatite grade.
- (3) Compelling evidence for escape of CO₂ from the mantle today.

Some problems with the hot-spot model are:

- (1) Although high CO₂ activity in the upper-mantle plume might be expected to produce some alkaline basalts⁵², these are almost unknown in the Archaeon³⁹.
- (2) Ancient tonalities are strongly depleted in heavy rare earths⁷⁴. Explanation in terms of residual garnet is not supported by too low seismic velocity in lowermost crust for abundant garnet, and modest amount of garnet in granulite nodules transported by kimberlites through shields. A proposal¹⁹ that heavy rare earths were depleted by complexing and vapour transport is not supported by experimental evidence on rare-earth partitioning between silicate melt and high-pressure CO₂-rich fluid⁷⁵. Crystallization of very abundant residual amphibole might alleviate this problem.
- (3) In western Greenland, both the 3,700 Myr Amitsoq and 2,900 Myr Nûk tonalites were partly metamorphosed into the granulite facies, and it is not clear how a single mantle reservoir could achieve this: however, continental drift and mantle convection might bring a second reservoir into position.
- (4) No explanation is given for strong horizontal tectonic movements during emplacement of tonalite gneisses (for example, Amitsoq and Nûk gneisses⁷⁶).

Plate-tectonic model

The margin of an Archaeon proto-continent (Fig. 2) consists of a magmatic arc coupled with a back-arc basin. A batholithic root becomes a high-grade granulitic belt after carbonic metamorphism, and basalts and graywacke detritus of the back-arc basin ultimately collapse into a greenstone belt as the island arc coalesces onto continental foreland⁷⁷. Altered oceanic basalts and sediments rich in H₂O and CO₂ undergo dehydration and

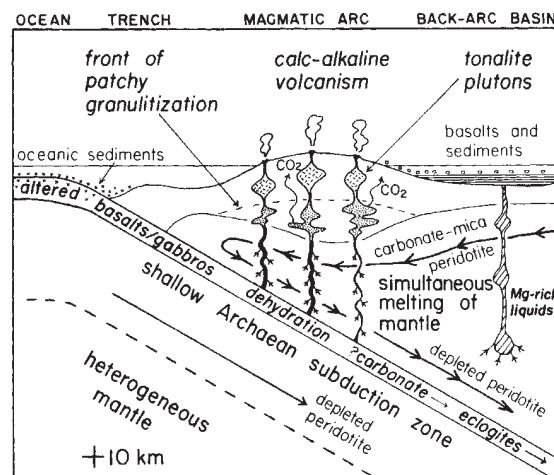


Fig. 2 Asymmetric plate-tectonic model for crustal growth and carbonic metamorphism. Subsequent compression converts the back-arc basin into a greenstone belt while the magmatic arc undergoes horizontal deformation to produce a high-grade region. Repeated under-riding of the subducted slab and coalescence of each back-arc basin and magmatic arc produces a complex terrain of greenstone belts and high-grade suites. In the subducted slab, dehydration occurs by loss of either a vapour or a liquid phase which passes into the mantle wedge. Some carbonate may survive with eclogite to become mixed mechanically with depleted peridotite. The volatiles from the descending slab interact with carbonate-mica peridotite in the mantle wedge to basaltic magma which mostly crystallizes in the base of the crust where amphibole retains H₂O. Carbon dioxide is released into a vapour phase which produces a front of patchy granulitization. Remelting of amphibole-rich rocks produces tonalitic magmas which transport H₂O in the liquid phase to higher levels, leaving a granulitic residue behind. Earlier igneous rocks underwent later carbonic metamorphism.

decarbonation reactions²¹ during shallow subduction to produce a devolatilized residue of eclogite with some surviving carbonate⁵⁶. Either magmas or vapours, or both, rise into the mantle wedge carrying mainly H₂O but with some CO₂. Heavy arrows indicate corner flow of the mantle wedge⁷⁸, and small arrows indicate melting simultaneously with devolatilization of the subducted slab and possible partial melting therein. The mantle wedge is assumed to provide more CO₂ than H₂O. Magmas, generally of quartz tholeiite, differentiate in the lower crust, leaving an amphibole-rich residue which retains water and augments rare-earth fractionation caused by residual garnet in the sinking slab. Magma differentiation produces tonalitic plutons and calc-alkaline volcanism. Release of CO₂-rich vapour in the lower crust, as for the plume model, produces a granulitic lower crust with a front of patchy granulitization. These processes are envisaged to occur quasi-simultaneously but unevenly over ~50 Myr as subduction varies. Finally, when the island arc coalesces with continental foreland, the supply of volatiles from the subducted slab dies away.

The above scheme is tectonically similar to one⁷⁹ for Mesozoic calc-alkaline volcanic-plutonic complexes of the western US in which a postulated basaltic underplate is covered by a 10 km granulite layer succeeded by a lower-grade terrain in which crowding of emplaced plutons caused lateral compression. In western Greenland, rising tonalitic plutons became emplaced along active thrust planes⁷⁶.

Alternative mechanisms for calc-alkaline magma generation are by direct melting of oceanic crust in the subduction zone and by direct melting of the overlying mantle wedge. Given the lack of experimental knowledge of melting in mafic and ultramafic systems with mixed H₂O and CO₂, and at relatively low pressures, as in a fast shallow convection system, these possibilities cannot be ruled out.

The relative supply of H_2O and CO_2 is extremely important for success of the plate-tectonic model. Recent mid-ocean basalts tend to absorb more H_2O than CO_2 , but the most altered ones can contain roughly equal amounts (~ 2 wt%)^{80,81}. Most CO_2 of a subducted slab probably derives from thin calcareous oozes which permeate brecciated basalts as a matrix in the uppermost part of Layer 2⁸². Amphibolitized gabbros of Layer 3 have very little CO_2 ⁸³. That ancient oceanic basalts may have absorbed more CO_2 than younger ones because of a higher atmospheric pressure is worth exploration. Nevertheless, it seems difficult to obtain a substantial CO_2/H_2O ratio for a subducting slab, and it seems necessary to appeal to the mantle wedge for the bulk of the CO_2 . Perhaps some carbonate survives in the subducted slab, and augments the mantle reservoir after mechanical mixing with depleted peridotite.

Attractive features of the plate-tectonic model are:

- (1) The general calc-alkaline composition of ancient gneisses is similar to that of the rocks of modern volcanic and batholithic arcs.
- (2) Young back-arc basins compare fairly well in rock types and overall chemistry with greenstone belts⁶¹. Although some chemical features differ⁸⁴, temporal evolution of the mantle rather than tectonic mechanism may be the principal cause.
- (3) Structural evidence for horizontal tectonics in ancient terrains suggests plate collision.
- (4) Replenishment of CO_2 under continents is provided by 'conveyor belt' action of the mantle wedge associated with the subducted slab.
- (5) Garnet-rich residues mainly in the mantle, coupled with amphibole precipitation in the lower crust, can explain rare-earth fractionation in the tonalitic gneisses.

As with the hot-spot model, unanswered problems exist in the plate tectonics model:

- (1) How can CO_2 remain stored in the mantle during transport under the back-arc basin into the mantle wedge? Should not the CO_2 have escaped with basaltic magmas into the back-arc basin which is supposed to become a greenstone belt?
- (2) How can complex sequences of greenstone belts and intervening high grade gneisses be developed? For the present model the most obvious mechanism is successive coalescence of volcanic arcs onto continental foreland; however, no lateral age variation in greenstone belt sequences has been found⁸⁵, and andesites, the characteristic rocks of modern island arcs, are apparently rare in some ancient greenstone belts (ref. 39).

Conclusions

It is important to explain the dryness and CO_2 -rich fluid inclusions of ancient high-grade terrains. Because these features occur in very diverse chemical compositions inherited from igneous and sedimentary parents, a metamorphic process is indicated. Experimental phase-equilibria require removal of H_2O from hydroxylated minerals in the lower crust (~ 20 – 40 -km depth) by a vapour with high CO_2/H_2O . Consequently carbonic metamorphism deserves detailed consideration. The volume of lower continental crust is so great, and the required ratio of CO_2/H_2O is so high, that a mantle source of CO_2 may be required. Carbonate-bearing peridotite is stable to higher temperature than mica-bearing peridotite deeper than ~ 100 km, and oxidation of carbon might provide another source of CO_2 . Rising basaltic magma containing both CO_2 and H_2O in solution should lose CO_2 to the vapour phase as the pressure falls below 20 kbar (~ 75 -km depth) while water can be retained either in magma or in crystallizing amphibole. It is assumed that rising CO_2 vapour will diffuse through rocks containing hydroxylated minerals and flush out the water to produce a residue of dry granulite until the vapour becomes too diluted in H_2O , or until CO_2 becomes captured by scapolite. Water trapped in amphibole in deep-crustal basalt may subsequently escape to the surface dissolved in remelted diapirs which undergo little reaction with existing rocks.

Because of the complexity of tectonic processes in the Archaean era before development of large continental masses,

there is unresolved speculation about the origin and development of high-grade regions and greenstone belts. Two simple models based on hot-spot and plate-tectonic features show how the concepts of carbonic metamorphism might be applied. Neither is fully satisfactory, but the models may prove useful for further discussion of Archaean geology.

We thank A. T. Anderson, R. A. Howie and P. J. Wyllie for helpful criticisms, but their endorsement of the present speculative ideas is not implied. The following grants are acknowledged: NSF EAR 78-15939 (R.C.N.), EAR 79-05723 (R.C.N.), and EAR 77-21700 (J.V.S.), NASA 14-001-171 (J.V.S.) and NERC GR3/3198 (B.F.W.). We thank S. Moorbath, P. R. A. Wells, G. N. Hanson and D. H. Eggler for their helpful comments.

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ARTICLES

Late Quaternary history of the Nile

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During the intertropical cold dry phase from ~20,000 to 12,500 yr BP, the aggrading Nile was a braided, highly seasonal river. With a headwaters change to warmer, wetter conditions, it became an incised, sinuous, suspended load river. Overflow from Lake Victoria and severe floods in Egypt heralded the change in Nile regime.

THE Nile dominates the northeastern quadrant of Africa, flowing 6,700 km from the glaciated highlands and montane forests of Uganda (4°S) through the alluvial plains and desert sands of Sudan and Egypt into the eastern Mediterranean (31°N, Fig. 1). Recently dated river and lake deposits in Sudan¹, Ethiopia² and Uganda³, and eastern Mediterranean deep-sea core data^{4–6} now allow us to present an integrated history for the entire Nile basin for the past 20,000 yr. It is now possible to reconcile the alluvial history of the main Nile^{7,8} with events in the rest of the basin⁹. We focus on the late Pleistocene dry phase (~20,000–12,500 BP) and the terminal Pleistocene to mid-Holocene moister interval (~12,500–5,000 yr BP). As these two intervals contrast strongly in climate, a coherent interpretation of former Nile regime must accommodate both.

Nile hydrology and headwaters

Key aspects of the present Nile hydrology^{10,11} are shown in Table 1. During the dry winter the White Nile provides 83% of main Nile flow and sustains it to the sea when the Blue Nile has fallen 15 m and the Atbara is dry. During the Ethiopian summer floods Blue Nile flow and suspended sediment concentration¹² increase 40-fold. The Blue Nile and Atbara then provide 90% of the flow and 96% of the sediment of the main Nile. Throughout the late Quaternary, the separate contributions of the White Nile and of the Ethiopian tributaries have to be borne in mind.

Of the two major lakes in the upper White Nile basin, Lake Victoria (Fig. 2) was without outlet for at least 2,000 yr before 12,500 yr BP and probably again, briefly, around 10,000 yr BP (ref. 13), but is unlikely to have dried out completely. Closure of Lake Victoria would have reduced White Nile flow and increased its seasonality. Lake Mobutu Sese Seko (Lake Albert) was closed from ~25,000 to 18,000 yr BP and from 14,000 to 12,500 yr BP (ref. 14), during closure of Lake Victoria. Except for these times, it communicated with the White Nile, maintaining winter flow.

Ruwenzori supported the second largest late Pleistocene ice cap in Africa (260 km²). Glaciers also developed on Mounts Kenya, Kilimanjaro, Elgon and the Aberdares. Estimates of mean snowline lowering on each mountain range from >480 to 880 m, corresponding to a temperature decrease^{15,16} of 3–6 °C if precipitation remained constant. In Lake Mobutu the diatom

flora suggests cooler conditions¹⁷ than today between 28,000 and 25,000 yr BP. If glacial maximum coincided with the minimum level of Lake Mobutu (25,000–18,000 yr BP), and rainfall was decreased by 25%, a temperature lowering of 6–8 °C would be likely³.

Pollen spectra from sites in East Africa point to a colder, drier climate than today between ~26,000 and 12,500 yr BP with highland assemblages dominated by small tree, shrub and grass pollen, indicative of widespread suppression of forest trees^{3,18}, and a vegetation more open than it is now^{19–21}. Cores from Lake Victoria¹³ show that lowland forest was either absent or of very limited extent in the White Nile headwaters between 15,000 and 12,000 yr BP. From 12,000 yr BP onwards equatorial and montane forest spread at the expense of grassland and woodland^{3,18}, presumably indicating warmer and moister conditions. Lake fluctuations between 26,000 and 12,500 yr BP were apparently more complex in equatorial Africa²² than in Ethiopia, and the overflow of Lake Mobutu¹⁴ between 18,000 and 14,000 yr BP suggests that glacial aridity here was less prolonged or severe.

The Atbara, Blue Nile and Sobat originate in the Ethiopian highlands (Fig. 1). Although little is known about the history of Lake Tana on the Blue Nile several lake basins in the Ethiopian and Afar Rifts adjacent to the Ethiopian highlands have been studied in detail, including Lake Abhe⁷ and the Rift lakes south of Addis Ababa⁹ (Fig. 1).

Lake Abhe, the terminal lake of the Awash River, fluctuates in response to hydrological changes on the eastern margin of the Ethiopian plateau as well as in the Afar depression. Lake Abhe was very high several times during the late Pleistocene and also

Table 1 Nile hydrology^{10,11}

	Discharge (km ³)	Sediment load (mton)	% of maximum monthly flow	% of minimum monthly flow
White Nile	27.5	2	10	83
Blue Nile	51.0	41	68	17
Atbara	12.5	14	22	0

processes^{1,2}. Small ice caps and cirque glaciers developed on the highest summits of Simen^{33,34}, Arussi³⁵ and Bale³⁶ mountains, indicating a snowline lowering³⁶ of 650–1,050 m. The Arussi Mountains were ice-free³⁷ by 11,500 yr BP, but the glacial maximum has not yet been dated. A temperature decrease of 4–7 °C is indicated by a downward shift of <1,200 m in the lower limit of active solifluction in the Simen Mountains^{36,38}, suggesting an extension of the high-altitude moorlands into the present forest belt, but there is insufficient evidence to confirm this hypothesis. Hamilton's studies³⁹ of post-glacial peats on Mt Badda (Arussi Mountains) show that towards 11,500 yr BP the vegetation was more open and more adapted to aridity than on any of the more southern East African mountains at that time

but recovery of the montane forest had occurred by ~8,000 yr BP in the Bale Mountains, and by 6,400 yr BP or earlier on Mt Badda.

The cold arid phase from near 23,000 to 12,000 yr BP probably also resulted in a reduction in vegetation cover at lower altitudes. The extensive distribution of poorly sorted colluvial deposits and alluvial fan gravel² suggests a general increase in erosion at this time. Modern experimental data show that deforestation of East African upland catchments results in a more rapid and more seasonal runoff regime and in a marked increase in sediment yield^{40,41}. Soil erosion would also have been accentuated by the spread of periglacial conditions at high altitudes^{1,36}.

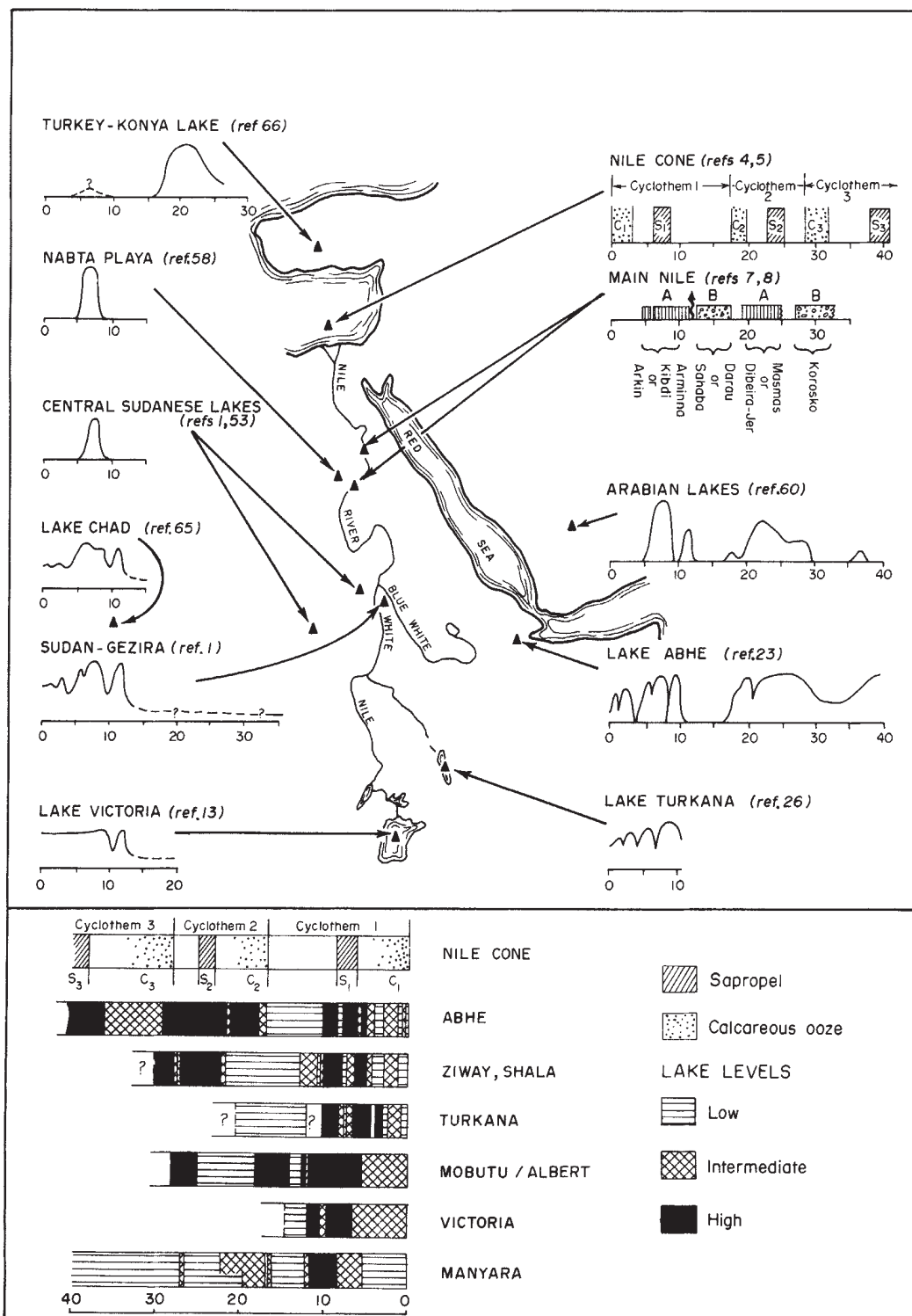
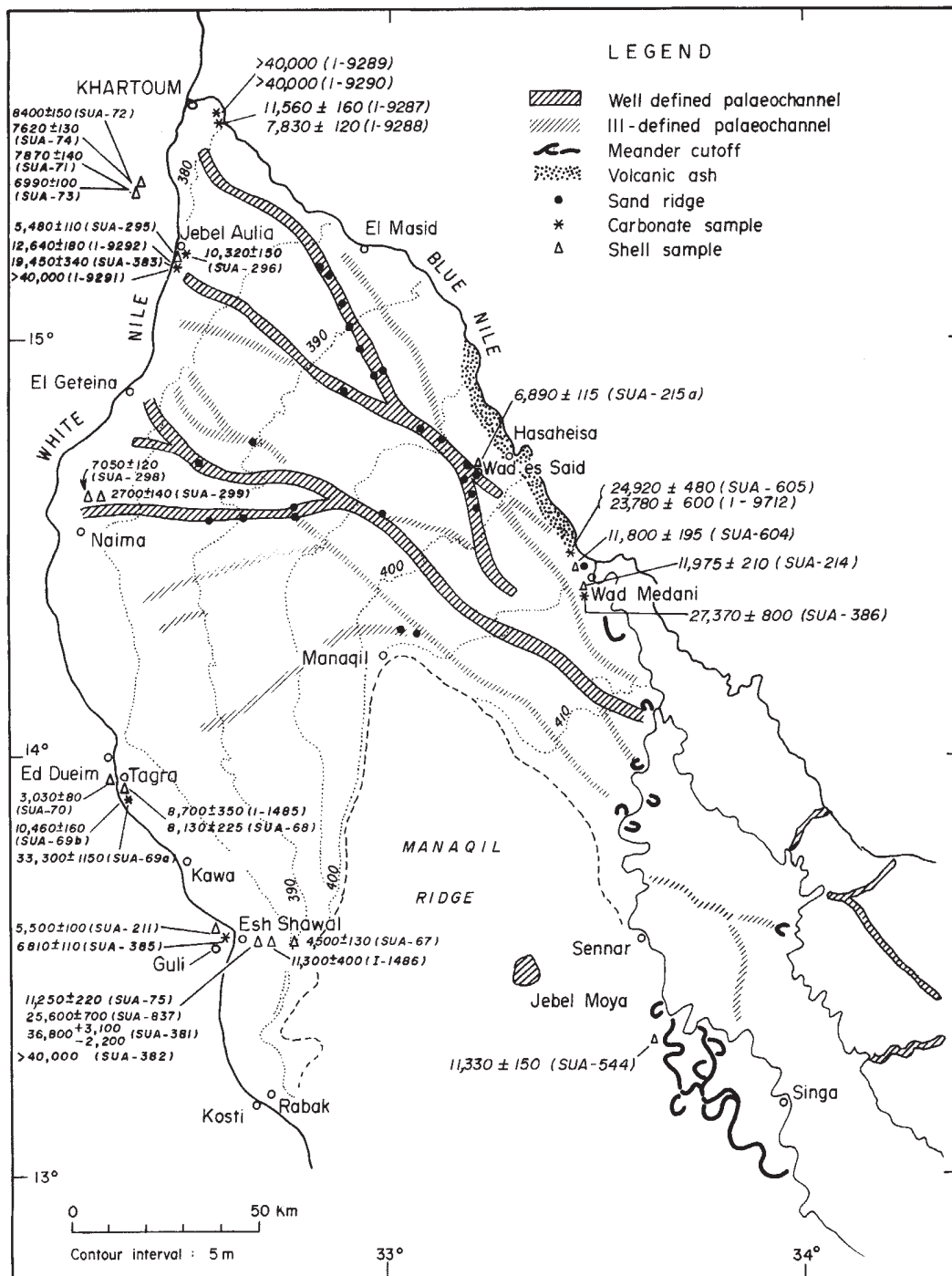


Fig. 2 Late Quaternary events in and around the Nile basin. (A, mainly Ethiopian flood silts; B, Ethiopian flood silts with sands and gravels; S, sapropel unit; C, calcareous ooze unit). Ages in kyr BP.

Fig. 3 The Blue and White Nile rivers, central Sudan, showing location of dated sites. Field mapping based on over 500 2-m boreholes and trenches.



The extension of closed vegetation types during the early Holocene was reflected in widespread slope stabilization in both highland and lowland areas. Consequently, the rivers transported predominantly fine-grained sediments and the clastic influx into the lakes was reduced by comparison with the preceding period. For example, the Meki River, which enters Lake Ziway from Ethiopian escarpment, began to lay down fine alluvial loams instead of coarse gravels.

We conclude that the phases of highest sediment yield from the Ethiopian highlands and lowlands corresponded to times of maximum aridity, minimum water yield, and highly seasonal runoff during the very cold late Pleistocene interval. These conditions dominated the fluvial regimes of the Blue Nile and Atbara rivers during the late Pleistocene arid period. In contrast, the terminal Pleistocene to mid Holocene was moister, the vegetation cover was more complete, slopes more stable, and sediment yield reduced.

Alluvial plains of the central Sudan

The alluvial plains of the lower Blue and White Nile rivers in central Sudan provide a depositional legacy of erosional events in their respective catchments⁴²⁻⁴⁴. A vast low-angle alluvial fan (the Gezira fan), up to 200 m thick and over 200 km in radius¹, was built up during the past 20 Myr (ref. 45) by ancient Blue Nile distributaries as they emerged from the Ethiopian highlands onto the plains of the Sudan. Our concern here is with the upper 4-5 m of this fan, which contains late Quaternary sediments from the two Niles (Fig. 3).

During a long interval dated^{1,46} at >40,000-25,000 yr BP evaporite deposits of microcrystalline dolomite and calcite accumulated along the White Nile near Esh Shawal. River sands which became progressively more clay-rich were laid down over the evaporites, and were in part reworked by wind to form dunes^{1,46} which were later flooded by the White Nile towards 12,000-11,000 yr BP. Radiocarbon ages of unbroken fresh-

water and amphibious mollusca indicate high White Nile flood levels towards 12,500–11,400, 8,400–8,100, 7,000, 5,500, 3,000–2,700, and 2,000–1,500 yr BP (Figs 2, 4). Excavations at Shabona^{47,48}, where small groups of elephant, buffalo and hippo hunters camped on low fixed dunes overlooking flooded White Nile swamps from which they collected abundant *Pila* snails dated to 7,000 yr BP confirmed that the White Nile floods were high towards 8,000–7,000 yr BP.

Figure 4 shows that high Blue Nile flood levels tally in detail with those of the White Nile for the intervals 12,000–11,000, 8,000, 7,000 and 5,500 yr BP. There is no evidence of extensive Blue Nile flooding in central Sudan after about 5,500 yr BP when the river entrenched some 10 m into its former floodplain^{49–51}. The dated Blue Nile high flood levels coincide with early to mid-Holocene high lake levels and higher water-tables in Ethiopia^{2,9,23,52}, with small lakes at En Nahud in Kordofan (6,800 yr BP)¹ and in Wad Mansurab basin 13 km north-west of Jebel Aulia⁵³ (Fig. 3) (8,400–7,000 yr BP).

Cross-bedded sands and gravels underlie the Blue Nile Holocene clays and occupy channel-fills within them. Borehole data reveal a change from a low-sinuosity bed-load regime to a high-sinuosity mixed- or suspended-load regime towards 12,000–11,000 yr BP (refs 1, 44), coinciding with forest expansion and slope stabilization in the Blue Nile headwaters.

Main Nile

The intricate response of different parts of the Nile basin to climatic change^{7,8,54–56} was first shown by studies of the alluvial stratigraphy of Upper Egypt and Nubia⁷. Here, Nilotic formations of late Quaternary age (Fig. 2) interfinger with local dune, wadi and pond deposits. Phases of aggradation by the main Nile were separated by episodes of rapid downcutting.

The oldest unit, the Korosko Formation⁷, consists of marls, gravelly marls, sandy gravels and Ethiopian silts deposited by a rapidly aggrading, braided Nile which was actively fed by local wadis. A probable minimum age of 27,250 yr BP has come from the upper part of this formation^{7,8}.

Aggradation of the Masmas Formation⁷ began long before 21,000 yr BP, and ended⁸ around 18,000 yr BP. The deposits comprise thick, horizontal flood silts of Ethiopian origin with occasional channel sands. They were laid down on a floodplain more than three times broader than today. Frequent crevasse splays suggest extensive seasonal flooding. Contemporary aridity in Nubia^{7,8,55,56} is indicated by dunes lining the west bank, which are dated^{57,58} at 19,000–17,000 yr BP. Local wadi activity was minimal.

During the Darau substage of the Gebel Silsila Formation⁷ (17,000–12,000 yr BP) vigorous braided channels existed on a floodplain twice as wide as today depositing a mixture of sands, gravels and Ethiopian flood silts. Exotic pebbles in the Darau Member as well as further upstream in Blue Nile deposits imply significant fluvial transport from Ethiopia and Sudan. At this time in Nubia and upper Egypt the wadis were intermittently active during the period 17,500–12,000 yr BP^{7,8} and pollen and diatom assemblages from permanent ponds indicate a locally cooler and effectively more humid climate than today. The Darau substage ended in a period of exceptionally high floods⁸ around 12,000–11,500 yr BP. Recent dates suggest that aggradation of mainly Ethiopian silts took place in the terminal Pleistocene to mid-Holocene intervals 11,200–9,300, 8,000–7,000 and 5,800–5,400 yr BP, with particularly high levels around 7,100 yr BP. Wadi deposits in Nubia indicate several phases of enhanced local runoff between ~11,500 and 5,000 yr BP. From 5,000 yr BP onwards, however, conditions in both Egypt and Nubia became increasingly arid^{7,8}.

Nile cone and eastern Mediterranean

Stratigraphic and isotopic evidence^{4–6} from eastern Mediterranean cores now allows partial separation of the effects of changes in river regime and sediment discharge^{8,54,59}.

Three recently recognized Nile cone cyclothem^{4,5} dated at 58,000–28,000, 28,000–17,000 and 17,000–0 yr BP are broadly coeval with the three alluvial formations in Nubia⁸. Each cyclothem comprises a sapropel unit, muds and turbidites, and a calcareous unit. The three sapropels coincide in time with high lake levels in the Nile basin⁹ and Arabia⁶⁰, and with the deposition of Ethiopian silts in central Sudan¹ and Egypt^{8,59} (Fig. 2). Sapropel 1 (9,000–7,000 yr BP) also corresponds with the early

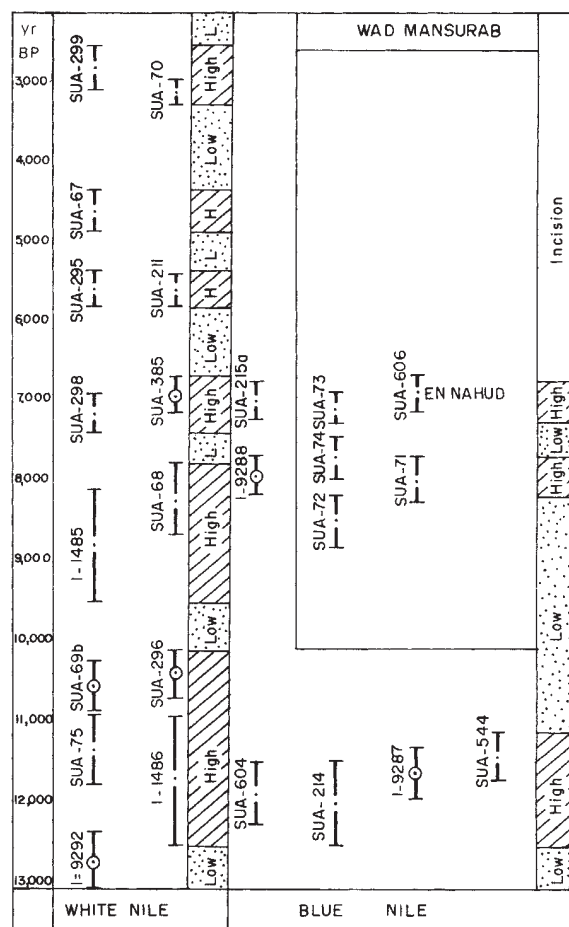


Fig. 4 Dated high Blue and White Nile flood levels in central Sudan. (All ages are corrected for isotopic fractionation; circles are pedogenic carbonates; dots are shells; bars represent 2 standard deviations.)

Holocene expansion of forest in the Nile headwaters³. The sapropels reflect stagnation of deep ocean water arising from a major influx of freshwater⁵ into the eastern Mediterranean from such sources as the Nile and Black Sea^{61,62}. The isotopic change evident towards 9,000–7,000 yr BP in core GA32 is best attributed to both a temperature increase and a freshwater influx^{6,61}. The periods of calcareous ooze accumulation^{4,5} correspond to times of aridity in the Nile basin. Stable isotope measurements in deep-sea cores from the eastern Mediterranean suggest that at the last glacial maximum, as at present, the eastern Mediterranean had an excess of evaporation over combined precipitation and river input (N. J. Shackleton, personal communication).

Evidence both from the eastern Mediterranean sea floor and from the Nile basin shows that in this region the interval 12,000–5,000 yr BP was generally moister than today and far wetter and warmer than the preceding late Pleistocene phase. Certain inferences may now be drawn about the late Quaternary Nile.

The 20,000–12,500 yr BP Nile

Cold dry conditions in the headwaters^{1–3,36} had profound effects on water and sediment supply to the Nile. Reduced vegetation cover, periglacial processes and summer snow melt gave heavy loads of coarse sediment. Flood peaks were high, annual discharge low. Episodic closure of the headwater lakes^{13,14} and consequent reduction in the area of swamps accentuated the seasonality of flow. The White Nile became a seasonal, intermittent river. Annual discharge from the Ethiopian headwaters diminished, so that flow along the main Nile was severely curtailed.

Along the lower White Nile bedload sands were reworked into aeolian dunes during the dry season⁴⁶. Distributaries of the Blue Nile radiated across the Gezira, also furnishing bedload sand for dune formation⁶³. The Atbara was even more intermittent than today. Summer floods were substantial, braided distributaries of the Blue Nile and Atbara spread fine gravels (including agate and chalcedony), sands and silts across their alluvial fans. Braided stream channels were characteristic of the main Nile in Egypt and Sudanese Nubia⁸, where mixed sediments similar to those upstream were also deposited. The sharing of flow among braided channels implies that the bedload was moved less efficiently than if flow were concentrated into one or two channels, with minimal frictional loss of stream energy. As flow ceased in the dry season bedload was locally reworked by wind. Channel instability was common during the flood seasons.

The 12,500–5,000 yr BP Nile

Following overflow from the headwater lakes and rapid expansion of swamps in southern Sudan, Nile flow became permanent and more regular. In the immediate aftermath of overflow from Lake Victoria towards 12,500 yr BP, there was major flooding along the White Nile¹. Full buffering by the Sudd swamps had not yet developed, so that vast quantities of water were released into the main Nile. The Blue Nile and Atbara also discharged high floods as rainfall increased in Ethiopia at this time. This

helps to explain the few centuries of extremely high floods⁸ in Egypt.

Thereafter permanent flow and much reduced seasonal fluctuation allowed the Nile to move its bedload along one or a few dominant channels. Regular Blue Nile floods laid down several metres of clay in the swampy plains of the Sudan Gezira^{63,64} and overbank floods deposited the Arminna/Kibdi silts on the narrow Egyptian floodplain⁸.

Conclusion

The fluvial response of the Nile to late Quaternary climatic changes in the headwaters helps to explain why rivers sometimes aggrade and sometimes degrade their floodplains. Between 20,000 and 12,000 yr BP when timberline in the headwaters was lower and the vegetation cover more open than today, the Nile was a highly seasonal braided river which brought mixed coarse and fine sediments down to Egypt and Sudan. This cold, dry interval had ended by 12,500 yr BP when overflow from Lake Victoria and higher rainfall in Ethiopia sent extraordinary floods down the main Nile, marking a revolutionary change to continuous flow with a superimposed flood peak. The main Nile and its tributaries established more stable channels of higher sinuosity, from which suspended Ethiopian silt and clay was deposited on the floodplains. The Blue Nile began to cut down, thereby depriving the Gezira fan of flood waters. By the mid-Holocene, the modern era of the Nile had begun.

Evidence from earlier periods is consistent with the above interpretation of the relation between Nile behaviour and environmental conditions in the basin (Fig. 2). The thick sequence of evaporite deposits and saline sediments on the lower White Nile also suggest earlier periods of desiccation and intermittent river flow which must have affected the main Nile. Study of the sediments beneath the Sudd and of the little known White Nile evaporites is required for the light they will shed on the earlier history of the basin.

We thank P. Goldberg, J. G. Jones and R. J. Wasson for discussions.

Received 30 June; accepted 27 August 1980.

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Integration of visual and auditory space in the mammalian superior colliculus

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Recordings of eye movements and single-neurone microelectrode recordings of the superior colliculus in cats show that, for each saccadic movement, their eyes start near to the centre of the orbit so that the coordinates of visual and auditory space are aligned, and complex neural compensation of auditory or visual inputs to the superior colliculus is unnecessary.

EYES and ears are specialized for detecting events at a distance. Both vision and hearing can be used to localize objects in external space—a function of utmost importance to any animal anxious to avoid its predators or discover its prey. One part of the brain, the midbrain tectum (which in mammals consists of the superior and inferior colliculi), seems especially concerned with the analysis of spatial information derived from both the eyes and the ears. In animals of diverse phylogeny^{1–6} there are neurones in the midbrain that have spatially restricted receptive fields in auditory or visual space and which respond when a sound or light stimulus appears (or preferably moves) within the appropriate, limited region of space. These systems of sensory neurones are topographically organized to form neural ‘maps’ of auditory and visual space across the midbrain tectum.

The idea that the roof of the midbrain is devoted to the analysis of positional information in external space is supported by the existence there in some species of other mechanisms for localization. The superior colliculus (SC) of cats⁷, mice⁴ and hamsters⁸, as well as having both visual and auditory input, has a topographical representation of the body surface including the whiskers; neurones in the inferior colliculus of the bat⁹ may play a part in echo location; and in the SC of the viper there is even a spatial representation of signals from the IR pit organs in the snake’s face¹⁰.

Damage to the tectum interferes with an animal’s ability to ‘orient’ towards stimuli: indeed, lesions of the hamster’s SC produce a visual defect that renders the animal seemingly blind to novel events in its visual field¹¹. In the cat, removal of one SC (which represents primarily the opposite half of space) produces neglect of the contralateral hemifields¹². Also, lesions of the colliculus in monkeys cause deficits in the timing of eye movements¹³.

Further evidence for the importance of the SC in initiating orienting movements towards sounds or sights comes from the fact that electrical stimulation of this structure in unanaesthetized animals elicits movements of the eyes, head, ears and body towards the opposite side of space^{14,15}.

Correspondence of visual and auditory representations in the superior colliculus

The integrity of the perceptual world clearly demands correlation of positional signals from all sensory systems and especially of messages from the eyes and ears. An animal must know that an object that it both sees and hears is a single thing at one place in space; responses initiated by either auditory or visual cues must be harmonized and coordinated.

The deep layers of the mammalian SC seem ideally equipped for the correlation of spatial cues from the eyes and ears,

for here there are superimposed auditory and visual representations^{7,8,16–18}. Neurones in the rostral part of the SC respond to sounds or sights directly in front of the animal, whereas for those further back, visual and auditory receptive fields are shifted into the contralateral hemifield of space. Indeed in cats, many individual cells receive both auditory and visual input¹⁶: the activity of such neurones could be thought of as providing pure, positional information regardless of the sensory channel mediating it.

In support of this concept, Wickelgren¹⁶, working on the deep layers of the SC in paralysed cats, found such bimodal cells to have their visual and auditory receptive fields (though large) well matched in their horizontal eccentricity in space. Each neurone responded to either a spot of light or a small sound source presented in one particular region of the field. Could such cells in the cat’s SC be responsible for the functional integration of visual and auditory space, triggering orienting movements towards peripheral objects whether identified by their visual appearance or by the noise they make?

The effect of eye movements: Pöppel’s paradox

This hypothesis, though attractive in its simplicity, is paradoxical. Cells are able to respond selectively to sounds at a particular position by using the relative timing or intensity of sound at the two ears as the cue to direction: the coordinates of auditory space are defined with respect to the ears and hence the head. The positions of visual receptive fields are, however, defined with respect to the retina. As the eyes can move in their orbits, the coordinates of visual and auditory space used by bimodal neurones should, as Pöppel¹⁹ has pointed out, be torn apart every time an eye movement occurs. Unless some compensatory process occurs, bimodal neurones in the SC should provide ambiguous directional information whenever the eyes are deviated from the straight-ahead position.

There are at least three possible ways in which each bimodal collicular cell might take account of changes in eye position: (1) The cell’s visual receptive field might move with respect to retinal coordinates by an angular distance equal and opposite to each eye movement, thus maintaining spatial correspondence with the auditory receptive field. (2) The cell’s auditory receptive field might move in space by an amount equal to each eye movement and in the same direction, to preserve the correspondence. (3) The auditory or visual input to the cell might simply be switched off whenever the eyes are significantly deviated from the central position, at which the auditory and visual receptive fields are aligned.

The first two possibilities seem implausible because they demand rapid and gross reorganization of the connections between the eyes or the ears and the SC each time the eyes move. The third hypothesis, which was not considered by Pöppel, is perhaps somewhat more likely. We have now examined this perplexing problem in alert cats.

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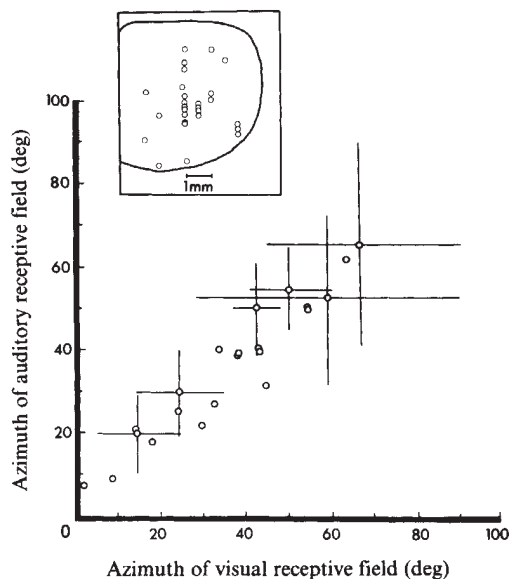


Fig. 1 The auditory and visual receptive fields of bimodal cells in the deep layers of the SC are roughly superimposed in space. The inset shows the recording sites (○) of 27 bimodal cells reconstructed with respect to electrolytic lesions and projected on to the horizontal stereotaxic plane within the outline of the right SC. The graph shows the azimuth angle of the centre of the auditory receptive field plotted against that of the visual receptive field for all 22 of the neurones that responded well to the stationary tone used to plot the auditory field. The cat's eyes were centred in the orbits and the head was fixed in the straight-ahead position. For six cells the horizontal extents of the visual and auditory receptive fields are indicated by horizontal (visual) and vertical (auditory) lines.

Testing the three hypotheses

For three adult female cats we used the techniques of Evarts²⁰ and Schiller and his collaborators²¹ to implant silver-silver chloride electrodes²² around the eyes (for recording horizontal and vertical eye movements electro-oculographically) and a chamber above the SC (for the introduction of glass-coated tungsten microelectrodes to record from single neurones).

We trained each animal to accept being wrapped in a cloth bag and to lie inside a padded box. Its head protruded through a large aperture and was attached to a superstructure that could be used either to measure horizontal and vertical head movements²³ or to fix the head in one position. With training the cats soon accepted these procedures.

To stimulate cells visually, a spot of light was back-projected on a translucent hemisphere (radius 57 cm) placed directly in front of the cat. Auditory receptive fields were plotted quantitatively by measuring the responses of cells to quiet tone bursts (duration 225 ms, frequency 1.2 Hz) emitted from a small radio earphone suspended from a crane whose centre of rotation was co-axial with the cat's head and whose angular position was varied in 10° steps over 180° in front of the cat and monitored by a potentiometer. The electro-oculogram (EOG) was calibrated^{15,24} and the position of the eyes was monitored as a two-dimensional display on a storage oscilloscope. For subsequent computer analysis, horizontal and vertical EOG signals were recorded on tape, together with the neurone's action potentials, the voltage corresponding to the position of the auditory stimulus and pulses to indicate each onset of the sound.

Precision of correspondence of visual and auditory receptive fields

We studied 27 bimodal cells (giving responses of roughly similar strength to optimal visual and auditory stimulation) in the deep layers of the SC. 50% of the cells recorded in the colliculus

below 1.2 mm from the surface were bimodal. The inset in Fig. 1 shows the position of each recording site at which a bimodal cell was found. With the cat's head held in the straight-ahead position, her attention was constantly attracted to the centre of the hemisphere, and fixation at the centre was constantly checked from the two-dimensional display of eye position. The position of the visual receptive field of the neurone was plotted by monitoring the responses elicited by a small moving spot (~2° in diameter) back-projected on to the hemisphere. Then the hemisphere was removed, all the room lights extinguished and the horizontal extent of the auditory receptive field plotted out by setting the height of the small loudspeaker on the same level as the middle of the visual receptive field, swinging the crane to various positions in front of the cat's head and recording the responses to tone bursts. Only five of the 27 bimodal cells could not be studied in this way because they failed to respond to the pure tone and were excitable only by more complex sounds such as key-jingling or finger-snapping.

Eye position was constantly monitored throughout this procedure. Rapid recalibration of the EOG, by the simple procedure¹⁵ of examining the range of signals produced as the cat made eye movements over the whole oculomotor range, showed little change in the d.c. level or gain of the EOG within the period of darkness in these experiments.

All bimodal cells were spatially selective in their responses to sound and visual stimuli, although in some cases, especially for cells in the more caudal part of the colliculus, representing the more peripheral field, visual and auditory receptive fields were rather large and their borders not sharply defined. However, we were satisfied that our data confirmed Wickelgren's¹⁶ observation that, with the eyes in a straight-ahead position, visual and auditory receptive fields are quite well aligned and usually of about the same horizontal extent. The graph in Fig. 1 plots the horizontal position of the centre of the auditory receptive field against that of the centre of the visual receptive field: total horizontal extents are also indicated for six typical cells.

Is there compensation of the visual receptive field during eye movement?

We did not attempt to measure possible minor variations in the dimensions, sensitivity or retinal positions of the visual receptive fields of bimodal cells during deviation of the eyes. However, for a number of bimodal cells we did informally replot the visual receptive field while attracting the animal's attention to various points on the hemisphere and hence producing deviation of the

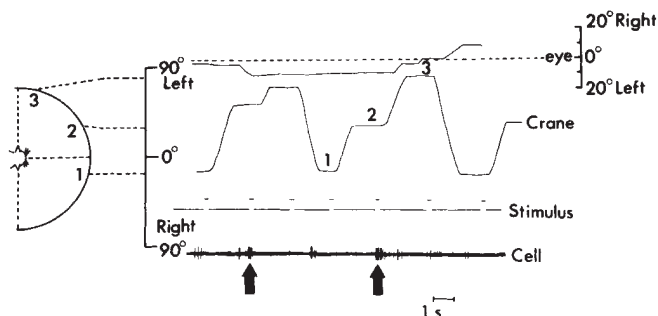


Fig. 2 A sample record from the experiment in which tone-burst stimuli were presented in the dark while the head was held. The position of the tone was randomized and the animal was encouraged to move her eyes. The top trace represents the horizontal eye position (approximate amplitude calibration on the right; interrupted line indicates the centre of the oculomotor range). The second trace shows the position of the crane that carried the loudspeaker (amplitude calibration on the left, with a sketch of the arrangement showing three positions labelled 1, 2 and 3, corresponding to the parts of the trace labelled). The third trace shows the duration of each 1.2 kHz tone burst (duration 225 ms). The bottom trace is an oscillograph recording of action potentials from a bimodal cell. Movements of the crane and noises produced by the experimenter elicited some activity between test stimuli. Clear responses to the tone are indicated by arrows.

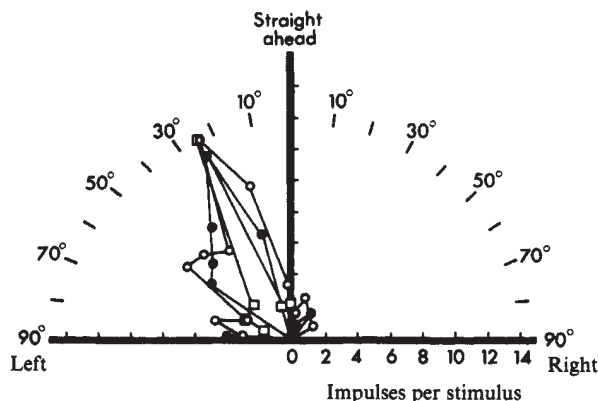


Fig. 3 Quantitative determinations of the spatial location and extent of the auditory receptive field of a bimodal cell. The visual receptive field for this unit was centred $\sim 25^\circ$ to the left of the vertical meridian of the visual field. Tone stimuli were presented randomly at different positions in front of the cat with the head held in darkness. The animal was encouraged to deviate her eyes. The response (mean number of impulses in the 500-ms period following the onset of the tone averaged over at least five stimulus presentations) is plotted along the radial axis of the polar graph. The average standard deviation is 2.7 impulses per point. The angle of this polar plot represents the angular horizontal position of the loudspeaker. Data are plotted for three conditions of eye fixation: eyes centred (within 7° of straight ahead; $\circ$), eyes deviated more than 7° right ($\square$) or left ($\bullet$). The auditory receptive field seems to be unchanged in spatial position and in sensitivity during deviation of the eyes.

eyes away from the central position. In no case was there any evidence of an obvious change in the retinal position of the receptive field: it always moved with the eyes and, except for possible brief changes in sensitivity associated with saccadic movements themselves^{15,25}, no bimodal cells seemed to suffer dramatic reduction in visual sensitivity during deviated gaze. We therefore reject the first hypothesis described above, as well as the possibility of strong attenuation of the visual input during deviated gaze (hypothesis (3)).

Is there compensation of the auditory receptive field during eye movement?

To test the second hypothesis we performed a detailed quantitative experiment on three bimodal cells (though the result was confirmed informally on many more). For each cell a series of ~ 500 auditory stimuli was delivered in total darkness with the cat's head held straight ahead and with the position of the crane randomly varied from tone to tone. We took care to deliver tones only when the crane was stationary and the room silent. In addition, between tone stimuli, the cat's attention was frequently attracted by tapping or speaking to persuade her to deviate her gaze away from the straight-ahead position. A commentary on the progress of the experiment was made on the voice channel of the tape recorder. Thus we randomized the position of controlled auditory stimuli while the eyes were sometimes straight ahead, sometimes deviated right, sometimes left.

Figure 2 is a typical example of the records obtained, showing eye position, crane position, sound stimuli and the activity of the cell. Note that although the cell was frequently active between the tone stimuli, in response to the relatively loud attention-attracting noises, only two of the tone bursts (marked with arrows) elicited clear responses.

In an off-line computer analysis, the responses of the neurone to tones at each position in auditory space were averaged for three ranges of gaze position: eyes straight ahead (within 7° of the resting position); eyes deviated $>7^\circ$ right of centre; eyes deviated $>7^\circ$ left. The data available allowed at least five responses to be averaged for every stimulus condition.

Figure 3 shows the results for one bimodal cell that had its visual receptive field centred about 25° left of the midline. Each point represents the average number of impulses in a 500-ms interval following the onset of the tone. Points are plotted on polar coordinates, the radial axis indicating the magnitude of the response. The data collected within each of the three ranges of gaze position are plotted with different symbols and clearly the maximum response was always of about the same magnitude and always occurred with the loudspeaker placed $\sim 25^\circ$ to the left of the midline, whatever the position of the eyes. The auditory receptive field did not move with the eyes, neither was the auditory input switched off when gaze was deviated. This result, which was reproduced in two other cells whose receptive fields were centred about 45° and 70° from the midline, seems to eliminate the remaining hypothetical forms of compensation described above.

For some cells the auditory receptive field was replotted with the head fixed not straight ahead but at a 45° angle to the right or left with respect to the body axis. In all cases the auditory receptive field shifted by precisely the same angle as the head. The auditory receptive field seems locked to head-centred coordinates, as one would expect if it depends on timing or intensity differences at the ears for its spatial selectivity. The auditory receptive field is not fixed with respect to the eyes nor with respect to the body axis as it does not move with the eyes when the head is stationary and it does move with the head when the head moves.

Recentering of the eyes during gaze shifts

Our results so far indicate that there is no simple mechanism in the cat's SC for compensating for deviations of the eyes. Indeed, we predict that cats might suffer perceptual misalignment of visual and auditory space when the eyes are fixating peripherally. However, further experiments have revealed that a simple motor strategy ensures that this situation very rarely occurs in normal, freely moving cats.

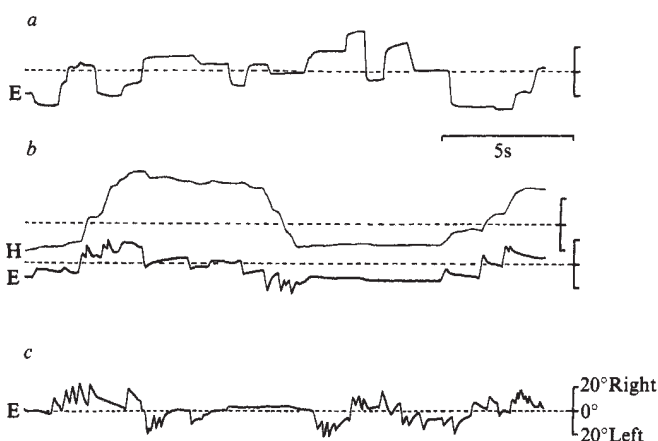


Fig. 4 Records of natural horizontal eye-in-orbit movements (E) and head movements (H) as a cat looks around a well lit stationary scene, in three conditions. The vertical calibration for each trace shows $\pm 20^\circ$ deviation from the straight-ahead position, which is indicated by an interrupted line. *a*, Head held stationary. The eyes make a series of characteristic saccades with intervening fixations, lasting up to ~ 2 s, with the eyes deviated up to $\sim 30^\circ$ from the centre of the orbit. *b*, Head free to move in the head-holder, which transduces head movements but impedes and slows them a little. Now each large eye saccade is accompanied by a head movement in the same direction. The vestibulo-ocular reflex evoked by each head movement results in a compensatory counter-rotation of the eyes, tending to bring them back towards the centre of the orbit. *c*, Head completely unrestrained (hence no trace for head position). Recentering of the eyes after each saccade is now even more efficient, indicating that the head usually executes a movement almost equal in amplitude to that of the eyes. Hence each new change of gaze starts with the eyes near the centre of the orbit.

In these three animals, and in three other cats implanted for EOG recording and head fixation, we used the methods of Blakemore and Donaghy^{23,24} to study coordinated movements of the head and eyes during changes of gaze. The superstructure to which the animal's head was fixed could be released to allow relatively free head movement, the horizontal and vertical rotations of which were monitored through potentiometers attached to the axes of rotation. We measured eye movements as the cat simply looked around the room in three conditions: head held still, head free to move in the headholder, and head completely unrestrained (Fig. 4).

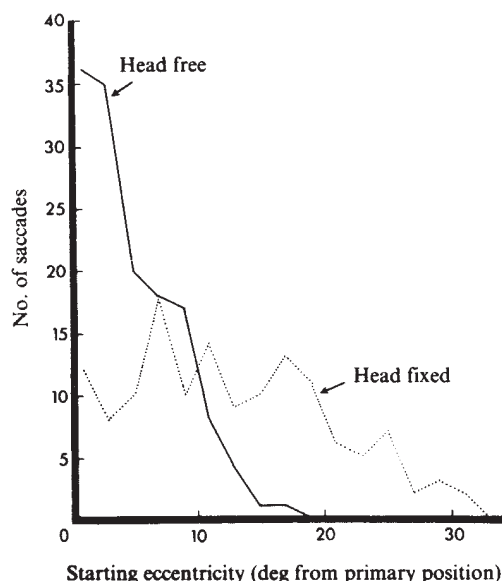


Fig. 5 Histograms showing the frequency of occurrence of eye-in-orbit position during steady fixation in head-fixed (interrupted line) and head-free (solid line) conditions (compare with Fig. 4a, c). The abscissa shows the horizontal position of the eye in the orbit (rightward and leftward deviations pooled) at the start of each saccade. Efficient recentering of the eyes in the head-free condition results in most new saccades starting with the eyes roughly centred in the orbit.

With the head held still the eyes make typical saccadic movements of up to $\sim 40^\circ$ amplitude with the eyes being held almost stationary for periods of up to 2 s, at deviations in the orbit of up to $\sim 30^\circ$ from straight ahead (Fig. 4a).

The situation is different when the head is allowed to move (Fig. 4b, c). Gaze changes of more than a few degrees in amplitude are now accomplished by combined movements of the eyes and head, with the eyes' saccade usually starting 25–50 ms before the start of the head movement^{23,24}. Large changes in the direction of gaze involve a staircase of saccadic jerks of the eyes superimposed on a large head movement. Whenever the head is in motion, a counter-rotation of the eyes in the orbit, of opposite direction to the head movement and of virtually identical velocity, is superimposed on whatever other

eye movement is occurring. Blakemore and Donaghy²⁴ and Donaghy²⁷ have shown that this counter-rotation of the eyes in cats is due to the accurate operation of the vestibulo-ocular reflex. This has the effect of slowing down the saccade if the head begins to move before the eye has reached its target, and of causing a compensatory eye drift in the direction opposite to the saccade as the head movement continues after the end of the saccade (Fig. 4b). As the head rotation is usually of similar angular displacement to the saccadic eye rotation it accompanies, the net effect is to return the eye close to its starting position shortly after each saccade.

The saccadic mechanism can be viewed as a rapid motor system for the fixation of objects of interest, but the complete gaze change in a cat nearly always involves a similar movement of the head that effectively recentres the eyes. Hence, whenever a cat is steadily fixating an object after a whole gaze change is complete, the eyes are nearly always close to the centre of their orbits. This is very clearly shown in records of horizontal eye position when the head is completely unrestrained (Fig. 4c). Nearly all steady fixations occur with the eye close to the orbital centre, and each new change of gaze starts from roughly the straight-ahead position.

Figure 5 plots as a histogram the horizontal starting positions of the eye in the orbit for 70 successive changes of gaze made by each of two cats as they looked around a stationary scene. With the head fixed, the distribution of starting positions has almost constant probability out to 20° deviation and some saccades started with the eyes deviated horizontally by more than 30° . On the other hand, with the head completely unrestrained more than half of all saccades started with the eyes less than 3° from straight ahead in the orbit and very few started with the eyes more than 10° from the primary position.

Paradox resolved for the cat, but not for primates

Pöppel's paradox¹⁹ turns out not to be a problem for the cat. Complex neural compensation of the auditory or visual inputs to bimodal cells is unnecessary because the motor programme used by the cat to look around ensures that the eyes rapidly return near to the centre of the orbit after each saccade. Every time a new peripheral object attracts the cat's attention its SC can safely assume that the eyes are near the primary position, and hence that the coordinates of visual and auditory space are aligned.

On the other hand, for primates, including humans, the paradox still remains. Quite clearly, monkeys and people do not follow every eye saccade with a head movement of nearly identical amplitude. Occasionally fixation is maintained steadily on a peripheral target with the eyes deviated by 40° or more. We know very little about the neural basis of sensory integration in monkeys (and even less, of course, in man) although bimodal cells have been described in the primate SC^{28,29}. The greater independence of the head movements in primates makes Pöppel's paradox a real issue once again.

This work was supported by grants 6973/447B and 6976/346 to C.B. from the MRC. L.R.H. and M.J.D. were MRC Scholars and C.B. held a Locke Fellowship from the RS.

Received 14 July; accepted 9 September 1980.

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Leaky +1 and -1 frameshift mutations at the same site in a yeast mitochondrial gene

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Two mutations in a mitochondrial structural gene, which cause leaky premature polypeptide chain termination and leaky growth, are +1 and -1 frameshifts in the same run of five T residues. The partial restoration of reading frame is probably due to ribosomal frameshifting at this site, and may be promoted by the unique structure of the yeast mitochondrial tRNA^{Phe} (ref. 1).

THE mitochondrial genetic system carries out the relatively limited task of making about 10 polypeptides. It has become clear recently that the genetic code specifying these polypeptides is somewhat different from the standard genetic code, and that there are even differences in the code between mitochondria in different species²⁻⁸. These differences could be due to the ability of mutations that change the code to be tolerated and fixed in a simple genetic system or due to some unknown selection for novelty. They might also reflect some primitive features of the mitochondrial genetic system.

To probe the nature of the mitochondrial genetic system further, we have continued to examine the DNA sequence of mutations in the yeast mitochondrial structural gene termed *oxi-l*, which codes for subunit II of cytochrome *c* oxidase^{3,9}. One specific aim of these studies is to investigate the possibility that some codons which do not occur in the wild-type gene might be untranslatable. For this reason we examined several mutations in the *oxi-l* locus that were previously reported¹⁰ to behave like leaky polypeptide chain terminators. Surprisingly, the leaky mutations examined so far have been found to be +1 and -1 frameshift mutations at a particular site in the structural gene. The findings indicate the existence of a mechanism that can promote frequent reading frame errors at specific sites during the expression of yeast mitochondrial genes.

The leaky phenotype

Among a recently described collection of some 90 *oxi-l* mutants¹⁰, five mutants were reported to have a leaky growth phenotype on medium containing non-fermentable carbon sources, and to synthesize greatly reduced amounts of cytochrome *c* oxidase subunit II. We have re-examined the phenotype of three of these mutants and have confirmed and extended the previous findings. When streaked on plates containing ethanol and glycerol as carbon sources, the three mutants M5661, M5701 and M5631 (Fig. 1c, e, g, respectively) grew significantly at 30 °C and 37 °C but not at 20 °C. In contrast, a non-leaky mutant (M13-249), shown previously by DNA sequence analysis to carry a frameshift, did not grow at any of these temperatures (Fig. 1b). In addition, spontaneous revertants of each of these mutants (Fig. 1d, f, h) grew similarly to wildtype (Fig. 1a). (Subsequent experiments demonstrated that the mutants M5661 and M5701 were independent isolates carrying identical lesions. Therefore, results are presented below only for M5701 and the third strain M5631.)

To examine the products of mitochondrial translation in these strains, yeast cells were treated with cycloheximide to inhibit cytoplasmic protein synthesis, and then labelled by incubation at 30 °C with ³⁵SO₄. Crude mitochondrial fractions were prepared

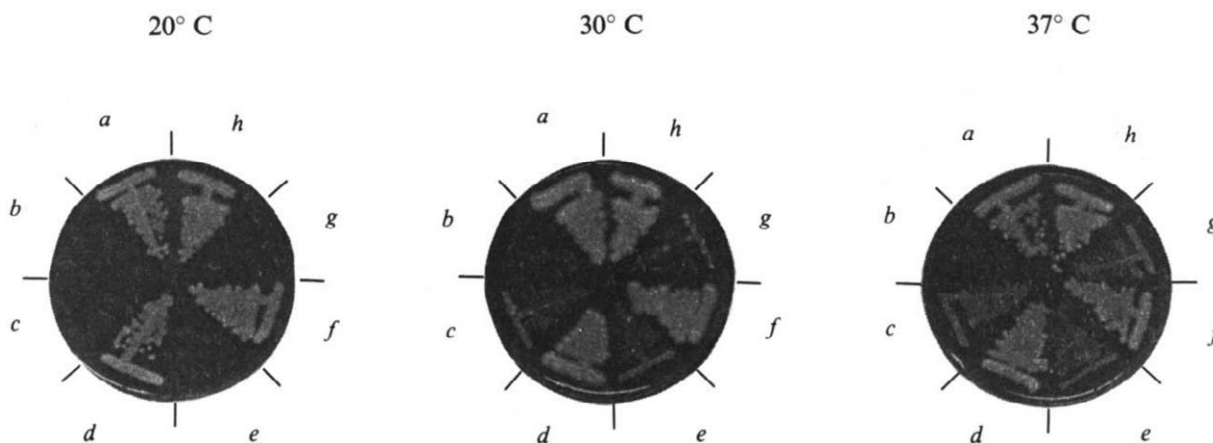


Fig. 1 Growth of wild-type, *oxi-l* mutant and revertant yeast strains on medium containing non-fermentable carbon sources. Plates containing 1% yeast extract, 2% peptone, 3% ethanol and 3% glycerol were streaked and incubated for 9 days at the temperatures indicated. The yeast strains were: a, wild type; b, M13-249, a non-leaky frameshift mutant^{3,26}; c, M5661; d, a spontaneous revertant of M5661; e, M5701; f, a spontaneous revertant of M5701; g, M5631; h, a spontaneous revertant of M5631. The mutants M5661, M5701 and M5631 were isolated from the haploid *pet*⁻ (*rho*⁺) strain 777-3A (ref. 10). To reveal the growth phenotype of these mitochondrial mutations and the wild type, diploids were formed from these strains by crossing them to a *pet*⁺ (*rho*⁰) tester strain. The resulting diploid strains, plated above and used in all experiments described here, are referred to by the original haploid names for simplicity. The spontaneous revertants were isolated from the diploid mutant strains.

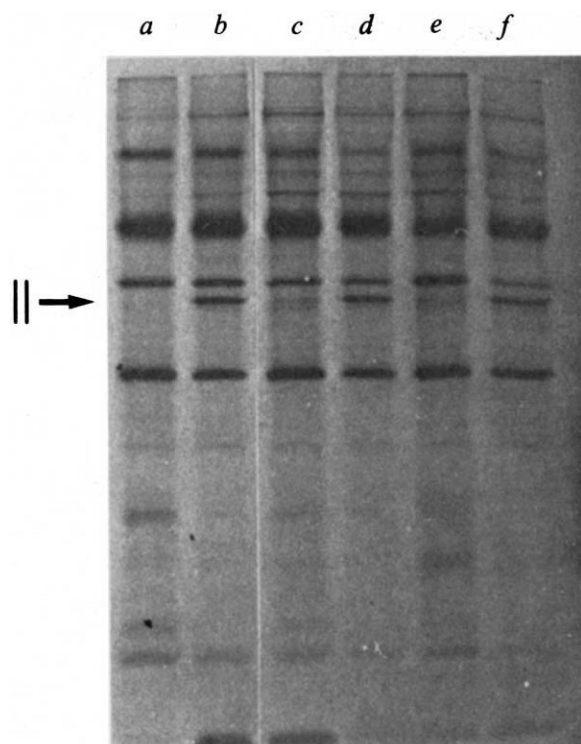


Fig. 2 Mitochondrial translation products of wild type, *oxi-1* mutant and revertant strains. Cells of strains M13-249 (a), wild type (b), M5701 (c), revertant of M5701 (d), M5631 (e) and revertant of M5631 (f) were labelled with $^{35}\text{SO}_4^{2-}$ in the presence of cycloheximide in medium containing 2% galactose as described²⁷. The mutant cultures contained revertants at frequencies $<5 \times 10^{-5}$. Mitochondria were isolated²⁸ and subjected to electrophoresis in a gel containing 15% polyacrylamide in the presence of SDS. The gel was dried and autoradiographed. The arrow indicates the position of cytochrome oxidase subunit II.

and subjected to SDS-gel electrophoresis. The mitochondrial translation products were visualized by autoradiography. The non-leaky mutant M13-249 failed to synthesize detectable amounts of cytochrome oxidase subunit II (Fig. 2a) as has been previously reported⁹. The leaky mutants M5701 (Fig. 2c) and M5631 (Fig. 2e), on the other hand, both produced small amounts of a polypeptide with the same electrophoretic mobility as wild-type subunit II (Fig. 2b). (A second polypeptide, moving slightly faster than subunit II, is also evident in these mutants and faintly visible in the wild type. As shown below, this protein is apparently not related to subunit II.) By densitometric scanning of autoradiograms, the amount of subunit II labelled in the mutants was estimated to be roughly 5% of that found in wild type at 30 °C. When cells were grown and labelled at 20 °C, the labelling of subunit II in the mutants was further decreased relative to wild type but was still detectable (not shown). Whether this further decrease accounts for the tight negative growth phenotype of the mutants at 20 °C is unknown. Labelling of subunit II was normal in the spontaneous revertants of both mutants (Fig. 2d, f).

To confirm that the faint bands observed in Fig. 2 indeed represented the cytochrome oxidase subunit, the labelled mitochondrial extracts were subjected to antibody precipitation with an anti-subunit II serum. SDS-gel analysis of the precipitates confirmed that the mutants M5701 and M5631 (Fig. 3c, e) had produced small amounts of the full-sized protein (molecular weight (MW) 27,000), whereas the non-leaky mutant (Fig. 3a) had produced none. In addition, a shorter polypeptide fragment was specifically precipitated from the extract of each mutant

(arrows in Fig. 3). These fragments can also be seen as faint bands in the total mitochondrial translation products¹⁰ (Fig. 2). In the case of the non-leaky frameshift mutant M13-249, the shorter fragment (MW 17,000) is known to result from termination at an out-of-frame nonsense codon downstream from the mutation³. As will be shown below, the fragments observed in the mutants M5701 and M5631 (MWs 9,600 and 12,500, respectively) are produced in a similar manner. One might therefore expect the labelling intensity of the mutant fragments to approximate that of subunit II in the wild type, correcting for the lower MW. However, the fragments are much less intense (Figs 2, 3). Possibly they are less stable than the wild type protein. A further caution regarding the quantitative interpretation of these autoradiograms is that the intensity of labelling in the presence of cycloheximide may not accurately reflect the relative level of proteins in growing yeast cells.

Several minor species are also present in the antibody precipitates of the wild type and revertants. In addition to small amounts of subunits I and III of cytochrome oxidase, at least four lower molecular weight polypeptides can be seen (Fig. 3) which seem to be related to subunit II insofar as they are very strongly reduced in the mutants. The origin of these smaller polypeptides is unknown.

Taken together, the above findings suggest that the leaky growth phenotype of mutants M5701 and M5631 is due to the

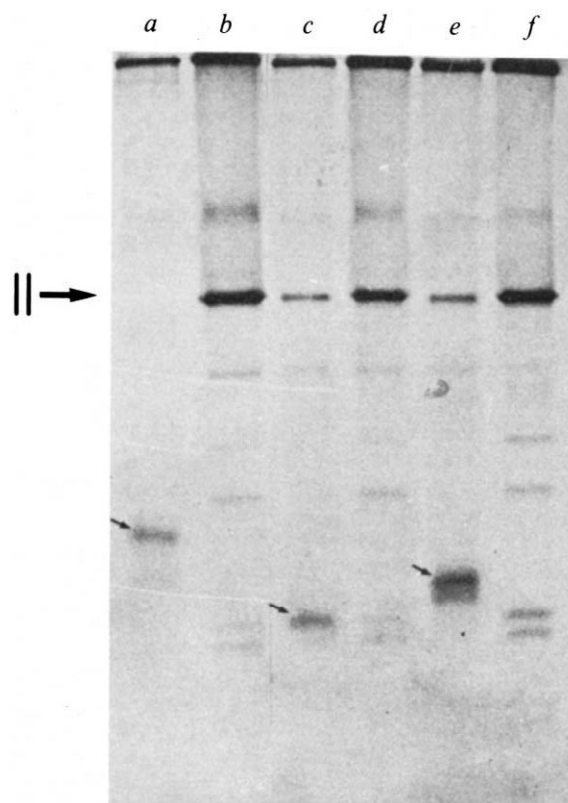


Fig. 3 Antibody precipitation of cytochrome oxidase subunit II and related polypeptides. The radioactively labelled mitochondrial translation products from the experiment of Fig. 2 were solubilized in SDS and subjected to immune precipitation²⁹ with a rabbit antiserum prepared against purified cytochrome oxidase subunit II (obtained from G. Schatz). The antibody precipitates were dissolved in SDS and electrophoresed on a 15% polyacrylamide gel which was dried and autoradiographed. As in Fig. 2 the labelled proteins were from M13-249 (a), wild type (b), M5701 (c), revertant of M5701 (d), M5631 (e) and revertant of M5631 (f). The position of subunit II in the gel is indicated, and small arrows in the autoradiogram indicate 'fragment' polypeptides specifically precipitated from the mutant extracts.

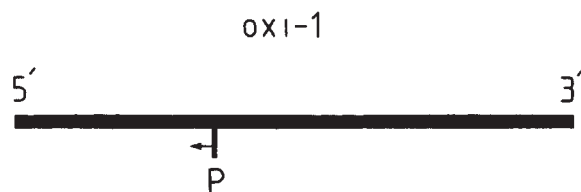


Fig. 4 Position of the mutations within the gene sequence. The horizontal line represents the sequence coding for cytochrome oxidase subunit II (753 base pairs), translated from left to right. The *PvuII* site (at position -147 in the sequence of ref. 3) utilized in the experiments of Fig. 5 is indicated by P, and the direction of sequencing by the arrow. The run of T residues affected by the mutations starts five base pairs upstream from the *PvuII* cut.

presence of reduced amounts of a functional form of cytochrome oxidase subunit II, and that this deficiency is caused by frequent premature polypeptide chain termination during translation of the protein.

Identification of frameshifts in the DNA sequence

To establish the nature of the mutations in strains M5701 and M5631, a 2,400-base pair *HpaII* restriction fragment that carries the entire *oxi-1* locus^{3,11} was isolated from the total mitochondrial DNA of each strain for sequence analysis. The positions of the mutations were estimated to be about one-third of the way into the gene based on the apparent MWs of the subunit II fragments observed. A *PvuII* cleavage site lies in this region³ (Fig. 4) and was utilized for end labelling and sequence determination by chemical degradation¹². Alterations in the DNA sequence of both mutants were found in a run of five T residues present in the wild type sequence immediately upstream from the *PvuII* site (Fig. 5a). In the mutant M5701, this run is shortened to four T residues by a single base-pair deletion (Fig.

5b) whereas in the mutant M5631 the run is lengthened to six T residues by a single base-pair insertion (Fig. 5d). Spontaneous revertants of each strain (Fig. 5c, e) were restored to wild-type sequence, indicating that no undetected second site mutations are present.

The predicted consequences of the -1 and +1 frameshifts for translation are shown in Fig. 6 based on the known sequence of the wild type gene³. Shortening of the T run (underlined) to four bases should lead to a TAA stop codon after the addition of two amino acids out of frame. Lengthening the T run to six should result in the addition of 29 amino acids out of frame, yielding a significantly longer fragment polypeptide. These predictions are in excellent agreement with the apparent MWs of the subunit II fragments detected in the experiment of Fig. 3.

Restoration of reading frame

The experiments described here show that despite the presence of a +1 or -1 frameshift mutation at a particular site in the yeast mitochondrial gene coding cytochrome oxidase subunit II, a significant amount of the full-sized gene product is formed. Thus, during the expression of these mutant genes, compensating errors must be made at or near the site of the mutations to restore translation to the proper reading frame. Although it is difficult to quantify accurately the frequency of reading frame restoration (see above), it seems to be roughly 5%. Leakiness of frameshift mutations in the β -galactosidase gene of *Escherichia coli* has been previously reported¹³. However, the levels there were 2 to 4 orders of magnitude lower than those described here.

The site affected by these *oxi-1* mutations is a run of five T residues. Whatever the mechanism that restores the reading frame, it is clearly site specific to some extent because at least one other frameshift mutation in this gene (a -1 mutation in a non-monotonous sequence) is not leaky (Figs 1-3 and refs 3, 9). Indeed, it seems likely that the compensating errors are made at the affected T run: eight of the 10 amino acid residues surrounding the site are identical in the yeast and bovine proteins^{3,14}, indicating that they have functional significance. If

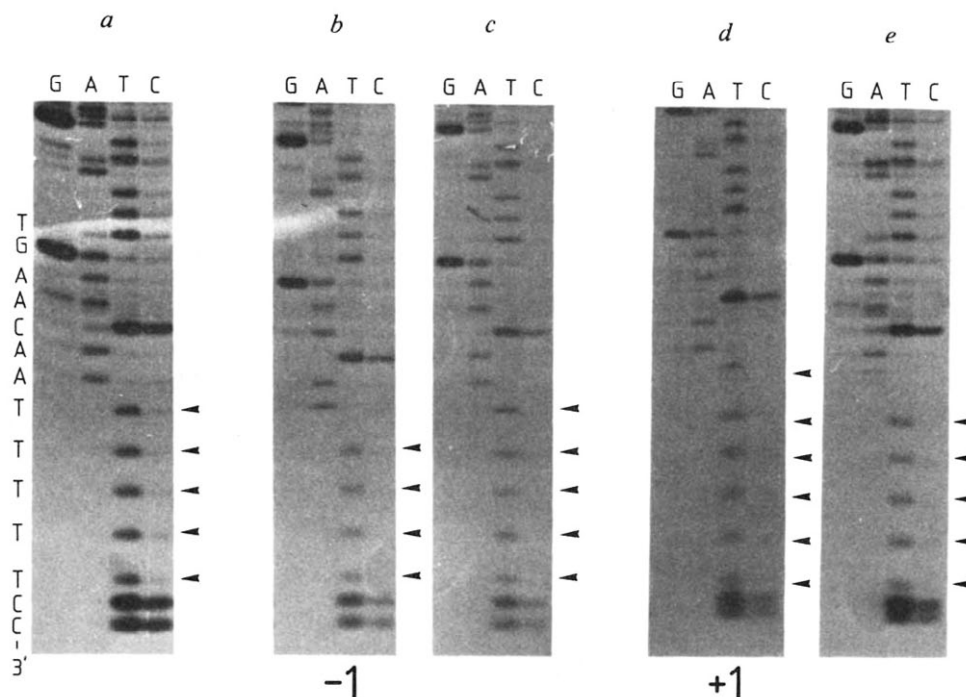


Fig. 5 Identification of a single base-pair deletion and a single base-pair insertion in the *oxi-1* locus of the leaky mutants M5701 and M5631, respectively. Mitochondrial DNA fragments labelled on the 3' end³ at the *PvuII* site indicated in Fig. 4, were isolated from wild type (a), M5701 (b), spontaneous revertant of M5701 (c), M5631 (d) and spontaneous revertant of M5631 (e), and subjected to chemical degradation sequencing reactions¹². Autoradiograms of the products after separation on 20% polyacrylamide gels are shown. The arrow heads next to the panels point to the T residues in the affected run. As indicated, M5701 is a -1 frameshift and M5631 is a +1 frameshift.

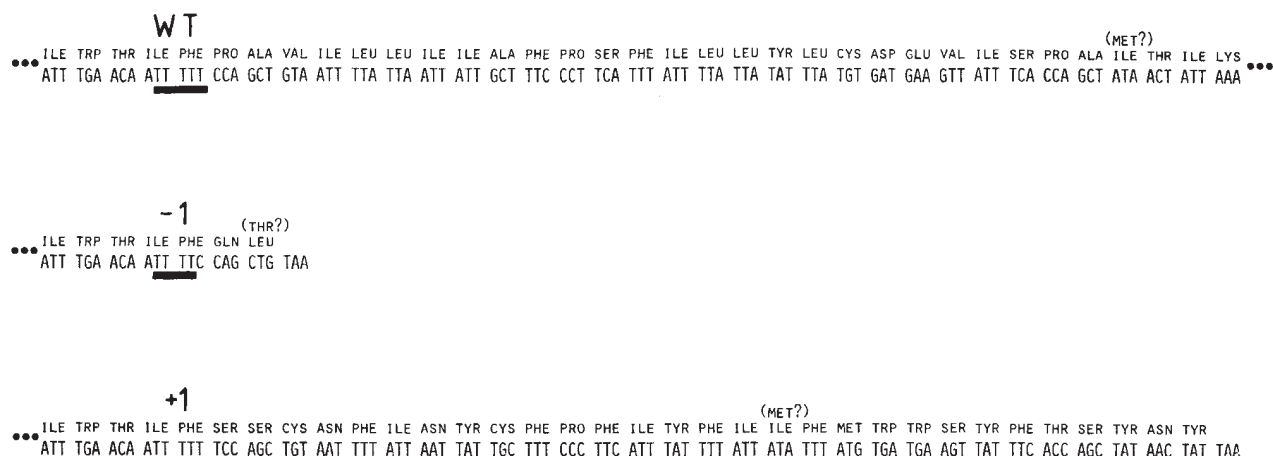


Fig. 6 Predicted translational consequences of the -1 and +1 frameshifts. A portion of the wild-type sequence (WT) (from ref. 3) including the site of the mutations (underlined) is shown. Out-of-frame translation beyond the mutations is shown up to the first termination codon encountered for the -1 and +1 mutations. Possible alternative codon assignments^{2,4} are indicated in parentheses.

compensating errors were made anywhere other than at the site of the mutations, at least some of this conserved amino acid sequence would be garbled.

It seems likely that a single mechanism underlies the reading frame restoration in both the +1 and -1 frameshift mutants. One scheme which immediately suggests itself would suppose that during translation of this monotonous sequence, a slippage of the ribosome and/or peptidyl-tRNA relative to the mRNA can occur in both directions. If, for example during translation in the -1 mutant, the ribosome were to slip back one nucleotide after peptidyl-transfer to the tRNA^{Phe}, the next codon exposed to the incoming aminoacyl-tRNA (CCA) would be in the wild type reading frame. Similarly, forward slippage would restore the wild type frame in the +1 mutant. In both cases, the peptidyl-tRNA^{Phe} would still be sitting on a Phe codon after the slip. A formally equivalent possibility would be that the ribosome occasionally translocates two or four nucleotides at this site. Similar but less frequent events presumably lead to the observed leakiness of +1 and -1 frameshift mutations in *E. coli*^{13,15,16}.

Several lines of evidence indicate that tRNA structures have an important role in maintaining reading frame during translation. First, mutated tRNAs are capable of suppressing +1 frameshift mutations both in bacteria¹⁷⁻¹⁹ and in the nucleocytoplasmic genetic system of yeast²⁰. The frameshift-suppressor tRNAs have generally been supposed to 'read' a 4-nucleotide codon, although it now seems that the actual mechanism may involve the induction of ribosomal frameshifting by the altered conformation of these mutant tRNAs^{16,21}. Furthermore, some normal tRNAs can also promote ribosomal frameshifting in both directions when added in excess to an *in vitro* translation system²². It is therefore very interesting that the wild type yeast mitochondrial tRNA^{Phe}, which is involved in translation at the site of the leaky frameshift mutations, has a unique structure:

the TΨC-stem contains an extra nucleotide which cannot be base-paired^{1,23}. This extra unpaired nucleotide surely affects the conformation of the tRNA, and it is tempting to speculate that the novel structure may either induce ribosomal frameshifting or promote the slippage of the peptidyl-tRNA^{Phe} relative to the mRNA. A precedent for this kind of hypothesis is provided by the case of the *E. coli* tRNA^{Trp} suppressor, in which a sequence alteration in the D-stem confers the ability to read UGA codons on an otherwise normal tRNA^{Trp} (ref. 24).

A somewhat different, and perhaps less likely model to explain the frequent frameshifting would suppose that the mitochondrial RNA polymerase occasionally 'slips' while transcribing a run of A residues, thus producing a small amount of wild-type mRNA from a gene carrying a frameshift. This hypothesis can probably now be tested using a heterologous translation system²⁵ programmed with mitochondrial mRNA from the leaky frameshift mutants.

Whatever the mechanism, it is clear from the results presented here that an extraordinarily high rate of reading frame errors occurs at specific points during the expression of at least some yeast mitochondrial genes. This obviously predicts that small amounts of prematurely terminated (and possibly extended) polypeptides should be synthesized by wild-type mitochondria as a result. Although we have not explicitly tested this prediction, it is not contrary to experience, in that many faint bands can always be detected in cycloheximide labelling experiments like that of Fig. 2 (see also Fig. 3). Such frameshifted proteins might be a burden tolerated by the cell. However, it is also possible that frameshifting at specific sites leads to the synthesis of physiologically important products.

We thank J. Wey and S. Stämpfli for technical assistance and R. Hall for a critical reading of the manuscript. B.W.-B. was supported in part by stipends from EMBO and Euratom. This work was supported by a grant from the Swiss NSF.

Received 1 August; accepted 26 August 1980.

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LETTERS

The Jodrell Bank radio-linked interferometer network

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The Multi Telescope Radio Linked Interferometer (MTRLI) has just been brought into operation at Jodrell Bank and here we introduce the instrument, describe its capabilities, and present some of the first maps to be made with it. MTRLI produces high quality maps of radio sources with resolutions varying from ~ 1 arc s to ~ 0.02 arc s depending on the frequency of operation. The obvious astronomical use of the instrument is for the mapping of powerful extragalactic radio sources to investigate the physical processes within them, but it will also have the capability to map galactic line as well as galactic continuum sources. The maps presented here were made at 408 MHz and are all of extragalactic sources. They illustrate the ability of MTRLI to map at low frequencies the steep spectrum emission which tends to be overlooked with existing synthesis instruments which have to work at much higher frequencies to obtain the same resolution.

The MTRLI which has been under construction since 1975 and is an extension of the long baseline interferometers first operated at Jodrell Bank¹ in 1954 over a baseline of 0.91 km (480 wavelengths). Subsequently the baselines were suc-

cessively increased by using radio links² to 127 km (2 million wavelengths) by 1967 (ref. 3). The present MTRLI concept was proposed in 1974 by Palmer as a further improvement and extension of these two telescope interferometer systems. The MTRLI uses one of the two large telescopes at Jodrell Bank, (the MK IA 76-m telescope or the MK II 25 $\times$ 37-m telescope) and the existing outstations at Defford and Wardle, together with three new 25-m telescopes sited at Knockin Darnhall and Tabley which are of the E-Systems design as used in the VLA. The first phase of the instrument using four telescopes is now working; the second phase in which the Darnhall and Tabley telescopes are added to the array will be complete by the end of 1980. When all telescopes are in use, data can be obtained from 15 baselines simultaneously ranging from 133 to 6 km in length. The system will be operated at a variety of wavelengths ranging from 73 to 1.35 cm, although at the higher frequencies not all telescopes are usable. Figure 1 indicates the position of the telescopes and the orientation of the baselines. The three new telescopes were sited to provide reasonably uniform coverage of the spatial frequency components of the sky brightness distribution. This is shown in Fig. 2 for declinations 10° and 50° north for the 15 baselines of the array. Because of the large N-S component in many of the baselines the resolution in the N-S direction remains comparable to that in the E-W direction even at low declinations.

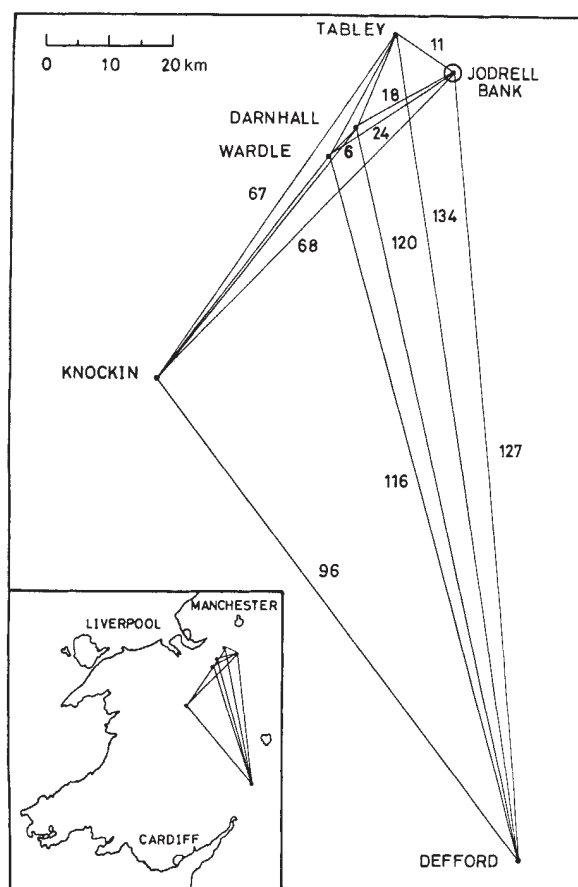


Fig. 1 The relative positions of the MTRLI telescopes with the baseline lengths given in kilometres.

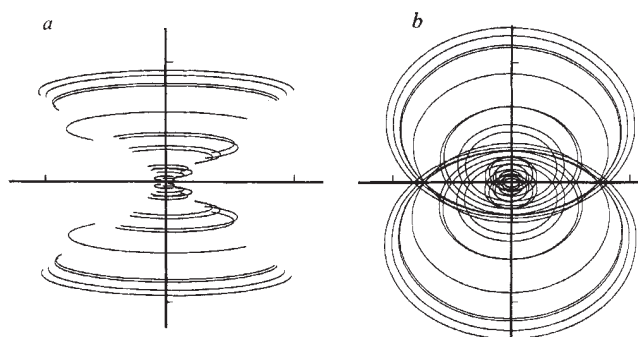


Fig. 2 The projected spacings of the MTRLI baselines for sources of declination: a, 10°; b, 50°. One division represents 100 km.

Each outstation telescope has an on-line computer to provide local control of the telescope and receiver or allow remote operation by land line from Jodrell Bank. Standard microwave links with a bandwidth of 10 MHz carry the radio signals from the outstations to Jodrell Bank, using two repeater stations in the case of Defford and Knockin, and direct for the nearer telescopes. Local oscillators at all sites are phase locked using a single frequency near 1,500 MHz. Pulses at this frequency are transmitted from Jodrell Bank to the outstations over the same paths as are used for the microwave links, locking high quality crystal oscillators at each repeater site and telescope. Pulses are then returned over the same paths and the received phase compared with that transmitted. In this way changes in the electrical path lengths are continuously measured with an accuracy of about 1 mm in 150 km, and corrections made to the phase of the received signals.

At Jodrell Bank the signals from each telescope are passed through phase rotators to remove the effects of the Earth's rotation, an analogue delay continuously variable between 0 and 75 ns and a digital delay of up to 1 ms in 50-ns steps to compensate for the varying geometry of the telescope baselines. The signals are then taken in pairs and correlated in a set of

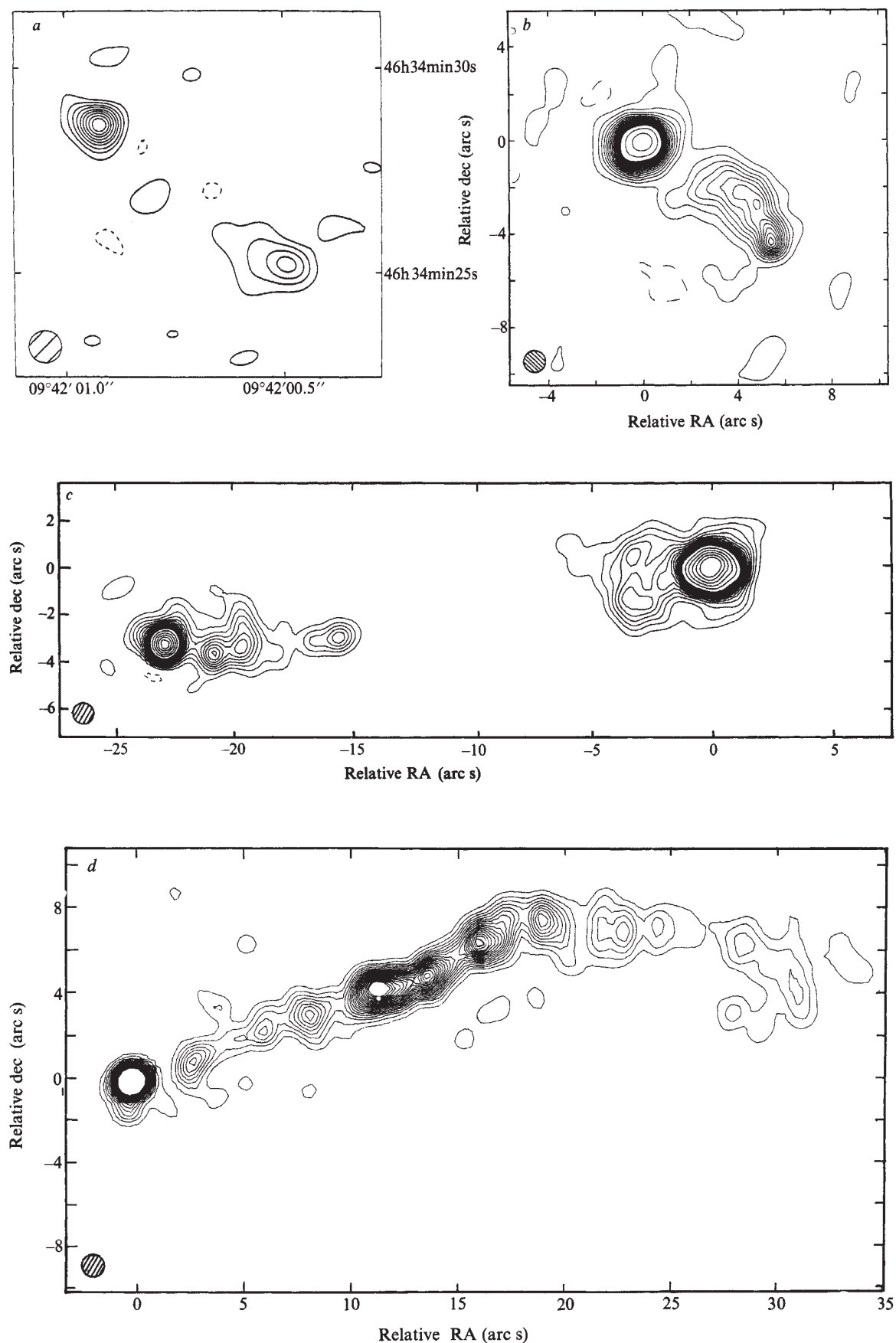


Fig. 3 The MTRLI maps. *a*, 5C5.168 at 408 MHz, the contour interval is 2 mJy per beam area. *b*, 3C153 at 408 MHz; the contour levels are 1, 3, 5...33, 35, 50, 75% of peak brightness; *c*, 3C249.1 at 408 MHz; the contour levels are 2, 4, 6, 8...28, 30, 40, 50, 60, 70, 80% of peak brightness. *d*, Virgo A at 408 MHz; the contour levels are 2, 4, 6, 8...38, 40% of peak brightness. The half-power beamwidth of the circular gaussian restoring beam is shown in each case in the lower left-hand corner.

one-bit correlators. These are normally connected as 16 complex correlators each with 32 channels of delay. If two or more sources are to be observed simultaneously in one telescope beam, the differential delay for the longer baselines may exceed the 32×50 ns available from one of these correlators. In this event the correlators can be connected together to provide fewer independent correlators with a larger number of delays. Integration over 1 s is performed within the correlators, and the data are then passed to a purpose designed computer where further integration, processing and storage takes place.

Sources are typically observed at all hour angles where the elevation remains above 5° and maps of the brightness distribution are produced by the CLEAN⁴ technique to remove unwanted sidelobe responses of $\sim 5\%$ caused by the incomplete spatial frequency coverage of the array.

The inherent phase stability of the interferometers and hence the map making capability of the system is fundamentally limited by the atmosphere above each telescope, with tropospheric effects being most important at high frequencies and ionospheric effects at low frequencies. These limitations may be overcome by determining the phase of the source being mapped relative to that of a nearby reference source. At low frequencies the source and a suitable reference can often be observed simultaneously within the telescope beam⁴, but at high frequencies it will be necessary to alternate between the source and reference on a time scale short compared with that of the fluctuations. Alternatively, with the sacrifice of positional information, one can produce maps which use the closure phase relationships⁶ between different combinations of telescopes. Cornwell and Wilkinson⁷ developed a mapping algorithm which corrects amplitude and phase errors arising at the separate telescopes in the array. This is exactly equivalent to using the closure amplitudes and phases as in the approach adopted by the standard 'hybrid' mapping algorithms of Readhead and Wilkinson⁸ and Readhead *et al.*⁹. The new algorithm is rather more general than these earlier ones and extensive tests on simulated data have shown that maps of complex sources made from typical MTRLI data are reliable down to $\sim 1\%$ of the peak brightness.

Observations of about 30 extragalactic sources were made during January and February 1980 at 408 MHz with a four-telescope array comprising the MK IA and the Wardle, Knockin and Defford telescopes. The observations provide an extreme test of the mapping ability of the system in that there were only six baselines available and the data were obtained in severe ionospheric conditions near the time of maximum solar activity. A full astronomical discussion of most of the results will be given elsewhere but we present in Fig. 3 a few of the maps produced from the observations to illustrate the capabilities of the system. The map of 5C5.168 was produced by reference to a source elsewhere in the beam, the remaining maps were produced using the new hybrid mapping technique.

5C5.168 (Fig. 3a) is one of four 5C sources mapped simultaneously using 5C5.175 as a reference source. This is a double source of 6 arc s separation with a total flux of 70 mJy. The contour interval is limited by noise at 2 mJy per beam area. Because an accurate position measurement for the reference source is available, the positions of the components of 5C5.168 are determined to ~ 0.2 arc s, but even with such accuracy the source remains unidentified on the Palomar Sky Survey down to 20th magnitude. The ability of MTRLI to map such weak sources means that we can investigate how the morphologies of radio sources depend on luminosity. This in turn is a prerequisite for the investigation of angular size evolution.

Figure 3b, and c shows maps of two high luminosity sources 3C153 and 3C249.1 respectively. The large dynamic range of the maps enables the details of the point features between the main peaks of emission to be seen clearly. Note that in both sources there is emission stretching from near the optical object out to just one of the lobes; in each case the second lobe appears completely isolated. Perhaps the emission is from the beam which is thought to transport energy from the nucleus to the

outer lobes, and then the asymmetry could be explained by relativistic beaming.

The map of Virgo A is included to illustrate how well MTRLI can map complicated sources with just four telescopes. That the details of the map are substantially correct is demonstrated by the coincidence of the radio and optical knots and by the good agreement found between the main features in the present map and that made with the VLA at 5 GHz (ref. 10).

MTRLI observations at 1,666 MHz of all the present sources are planned and detailed astrophysical discussion of the combined 408- and 1,666-MHz observations will be given elsewhere.

The construction of the MTRLI has involved major effort by many members of staff at Jodrell Bank, but we particularly thank J. A. Battilana, M. Bentley, A. Brown, D. C. Brown, R. D. Davies, R. J. Davis, M. Doggett, J. S. Haggis, J. Hopkins, R. G. Noble, H. P. Palmer, L. Pointon, R. S. Pritchard, D. Stannard and P. Thomasson.

Received 14 July; accepted 18 September 1980.

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Rotationally symmetric structure in two extragalactic radio sources

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Many extragalactic radio sources exhibit radio structures with some degree of rotational symmetry^{1,2}, which in extreme cases (for example, 3C315 (ref. 3) and NGC326 (ref. 4)) suggests precession of the source axis, such as might result if a relativistic beam of particles^{5,6} or stream of plasmoids⁷ were to change its orientation during the source lifetime¹. In such circumstances we might expect radiative and other energy losses to steepen the spectrum of the older regions of emission⁸ away from the current sites of activity, and so make them more prominent on low-frequency maps of the source structure. The new multi-telescope radio-linked interferometer (MTRLI)⁹ at Jodrell Bank was used during January and February 1980 at a frequency of 408 MHz to map the extragalactic radio sources 3C196 and 3C305 with a resolution of ~ 1 arc s. We show here that both the markedly symmetric structures observed and the spectral index distributions inferred from comparison with previously published 5-GHz maps¹⁰ provide evidence for the source axes having rotated during the lifetime of the emitting regions.

The sources were observed using four telescopes of the MTRLI, with projected interferometer spacings ranging between ~ 15 and 127 km. Over such distances the effects of ionospheric disturbances at the low observing frequency are large and the absolute phase information was not recoverable. Consequently, the closure-phase hybrid mapping technique described by Readhead and Wilkinson¹¹ was used, though with a significantly improved algorithm¹². The absolute positions of the components on these maps, lost in the hybrid mapping technique, were inferred from a comparison with the Cambridge 5-GHz maps. The main characteristics of the two sources are given in Table 1.

Table 1 Some relevant characteristics of 3C196 and 3C305

Source	3C196	3C305
Optical identification	18 m OVV quasar	13.5 mag Sa pec galaxy ¹⁴
Redshift	0.871	0.0416
Radio structure at 5 GHz (ref. 10)	2 main components. Third weaker component at 90° to source axis from N main component	2 main components surrounded by an extended low-brightness region
Separation of 2 main components	5 arc s	3.4 arc s
Projected linear size	43 kpc	3.8 kpc
Overall radio spectrum	Power law $\alpha = -0.81$	Power law $\alpha = -0.86$
Integrated radio luminosity	4.2×10^{45} erg s ⁻¹	1.8×10^{42} erg s ⁻¹

* Assuming $H_0 = 50$ km s⁻¹ Mpc⁻¹ and $q_0 = \frac{1}{2}$.

The MTRLI map of the high luminosity radio source 3C196, a quasar, is based on 16-h observation and is shown in Fig. 1. The projected linear size of the source is ~ 50 kpc. Components A and B are assumed to correspond to the main components on the Cambridge 5-GHz map. Component B' is identified as the third component on the Cambridge map, and is revealed to be an extended region of emission with a steep spectrum. Component A', which was not detected at 5 GHz and therefore has a steep spectrum, is a much weaker extended region, with a slight plateau at some distance from component A. A line drawn from this plateau to the peak of component B' passes through the position of the optical object. The physical properties of the components are listed in Table 2. Note that component A is significantly more extended than component B. The spectral indices of the components have been obtained by comparison with other published^{10,13} data. Note that in addition to the spectral differences between the compact components A and B in 3C196, the extended components A' and B' display markedly different morphologies and luminosities which may indicate time-dependent asymmetry in the power supply mechanism. Planned observations with higher resolution should enable this aspect of the source properties to be investigated.

The source 3C305, which is highly unusual for a 3C source in being identified with a 13.5 mag Sa peculiar galaxy¹⁴ of dimensions $\sim 20 \times 30$ kpc, is a relatively low-luminosity radio source, and the two compact components are separated by a projected linear distance of only 3.8 kpc. A strong absorption lane crosses the body of the galaxy at an oblique angle, and there is a region of O II [$\lambda 3,727$] emission centred in a position 3 arc s to the NE of the nucleus¹⁴. The MTRLI map of 3C305, based on 24-h data, is shown in Fig. 2. The rotational symmetry displayed on this map is striking. The extent of the low brightness regions A' and B' may be somewhat greater than is shown because only 85% of the total flux has been accounted for in the map. The spectral indices of the two main components and extended regions are given in Table 2. The apparent symmetry in this source is greater than in 3C196 because the intensity ratios A:A' and B:B' are similar. Component C is a possible candidate for a compact source associated with the optical nucleus of the galaxy. If this is the case, the region of O II [$\lambda 3,727$] emission lies close to the strong component B, but the uncertainty in the optical position prevents positive association.

In both 3C196 and 3C305, the rotational symmetry and the steep spectral indices (normally associated with the ageing of synchrotron electrons) of the extended components suggest that the axes of the radio sources have changed their orientation relative to the medium in which the sources are embedded. Hitherto, examples of such symmetry have been confined to

sources of large linear extent and relatively low luminosity. Thus these sources are very unusual not only for the degree of symmetry displayed, but also because they are small in linear size, and because 3C196 is an exceptionally powerful source.

Clearly, it is important to know the time scale on which such a rotation of the axis occurs. However, the determination of such a time scale is hampered by our ignorance of the physical conditions prevailing in and around the radio source components, and our lack of understanding of the mechanisms governing source evolution.

For component B' in 3C196 the spectral information in Table 2 allows us to make a rough estimate of the cut-off frequency ν_c , above which we expect the spectrum to steepen markedly due to the energy losses of the radiating electrons⁸. If we assume that these energy losses are purely radiative, we can deduce how long the component has been radiating without any fresh input of high-energy electrons. This time is $\sim 2 \times 10^5$ yr, which is thus the corresponding time scale t for the rotation of the source axis. The accuracy of this estimate depends critically on the validity of neglecting both adiabatic expansion losses and particle re-acceleration gains.

If we accept that in 3C196 the energy supply from the quasar was once directed at component B' and is now directed at component B, it is reasonable to assume that in the past, component B' was a similar distance from the QSO as component B is now. Because component B' is now only slightly more distant from the QSO than component B, it cannot have moved by more than ~ 10 kpc in the time taken for the source axis to swing through 65°. By assuming (1) that component B' is confined by ram pressure and (2) that the average internal energy density of the component during this period was no lower than it is now, we can deduce the minimum velocity of the component through the intergalactic medium which is required to confine it. Assuming an upper limit for the density of the intergalactic medium¹⁵ of $\sim 10^{-27}$ g cm⁻³, we find that a velocity of $\geq 0.03c$ is required to confine the component by ram pressure, and so the time scale t for the source axis rotation is $t \leq 10^6$ yr.

The rate of advance of a component through the surrounding medium deduced from the internal energy density of that component may enable us to set a lower limit on the time scale for the source axis rotation at present. From the appearance of component B' in 3C305 and the apparent gap between

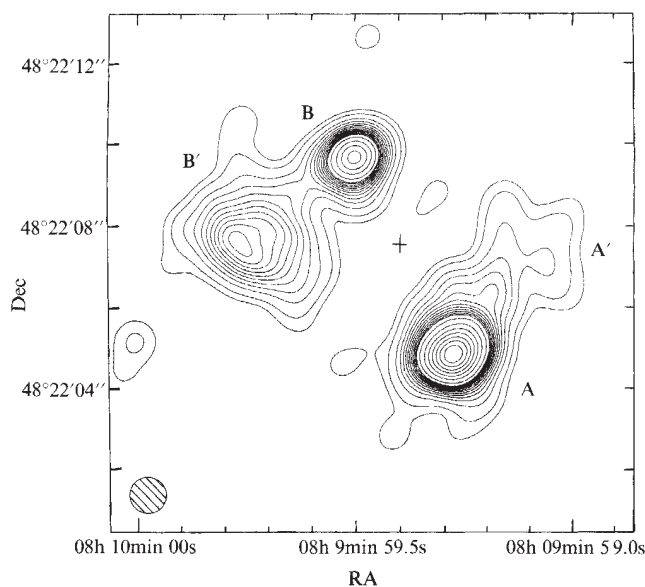


Fig. 1 The MTRLI map of 3C196 at 408 MHz. The contour levels are 1, 2, 4, 6... 24, 30, 40... 90% of peak brightness. The HPBW of the circular gaussian beam is shown in the bottom left corner. +, The position of the 18-mag quasar.

Table 2 Physical parameters of components in 3C196 and 3C305

Component	α_{408}^{5000}	$\pm$	α_{5000}^{15000}	$\pm$	Size (kpc)	$E_{\min}^{\text{tot}}$ (erg)	B_{eq} (G)	T_{sp} (yr)
3C196								
A'	<-1.0	—	—	—	12×10	—	—	—
A	-0.72	0.05	-1.05	0.06	6×4	3.0×10^{58}	3.7×10^{-4}	4.6×10^4
B	-0.60	0.09	-0.69	0.06	<2×4	$<8.1 \times 10^{57}$	$>4.7 \times 10^{-4}$	$<1.8 \times 10^4$
B'	-1.21	0.15	<-1.5	—	16×13	1.6×10^{59}	1.7×10^{-4}	2×10^5
3C305								
A'	~-1	—	—	—	~2.8×1.1*	—	—	—
A	-0.62	0.09	-1.35	0.23	0.9×0.9	2.6×10^{55}	1.2×10^{-4}	4.4×10^5
C	—	—	—	—	<0.5×<0.5	—	—	—
B	-0.72	0.06	-1.15	0.09	0.75×0.75	3.6×10^{55}	2.0×10^{-4}	2.0×10^5
B'	~-1	—	—	—	~4.8×1.1*	—	—	—

* Approximate values only, see text.

The spectral indices are defined in the sense $S \propto \nu^\alpha$. The sizes given are the dimensions of an equivalent gaussian. The minimum energy was calculated assuming that there are no relativistic protons, and assuming cylindrical component geometry. Equipartition of energy between relativistic particles and magnetic field was also assumed. The spectral age T_{sp} was calculated by assuming that spectral steepening is caused only by radiative energy losses, and by estimating the cut off frequency ν_c from the spectral data. Assuming $H_0 = 50 \text{ km s}^{-1} \text{ Mpc}^{-1}$ and $q_0 = \frac{1}{2}$.

components B' and B in 3C196, it is reasonable to suppose that the beam may have been switching on and off. If the source axis rotated through a significant angle whilst the beam was switched off, it would then have to re-excavate a channel through the surrounding medium, and this would take place at the above mentioned rate. Clearly, during the time taken for this excavation, the axis cannot rotate by more than the angle subtended between two discrete emitting regions. Assuming for 3C196 a typical intracluster medium density of $\sim 5 \times 10^{-28} \text{ g cm}^{-3}$, and for 3C305 (because it is embedded in the galaxy) a typical interstellar medium density of $\sim 10^{-25} \text{ g cm}^{-3}$, we find that the present rotation time scale for 3C196 is $t \geq 10^6 \text{ yr}$ and for 3C305 is $t \geq 5 \times 10^6 \text{ yr}$. If the assumptions inherent in these values are valid, this may indicate that the rotation rate in 3C196 has slowed down.

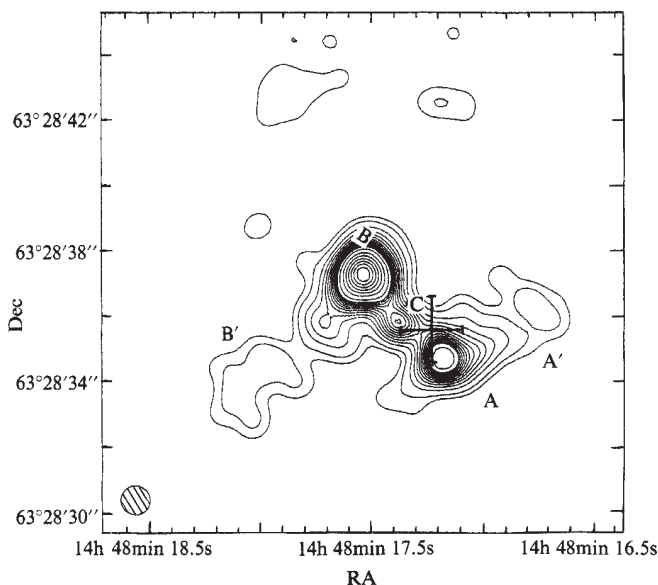


Fig. 2 The MTRLI map of 3C305 at 408 MHz. The contour levels are 1, 2, 4, 6...24, 30, 40, 50, 60, 70, 80, 90% of peak brightness. The HPBW of the circular gaussian beam is shown in the bottom left corner. +, The position of the nucleus of the galaxy.

The time scales we find for the rotation in these sources are very much shorter than those typically deduced for the larger sources. For example, Ekers *et al.*⁴ arrive at a value of $\sim 2 \times 10^8 \text{ yr}$ for NGC326, and this difference may indicate that the size of a source such as 3C196 is limited by the rapid rotation. Alternatively, we may be seeing the results of two completely

different mechanisms for producing the rotational symmetry. Ekers *et al.*⁴ mention that the precession of gaseous disk in the galaxy would probably lead to a long time scale. We will briefly consider an alternative mechanism that seems capable of producing a more rapid rotation.

Rees¹⁶ has discussed the possibility that the Bardeen-Peterson¹⁷ effect couples the radio axis to the rotation axis of a massive black hole at the centre of a galaxy, thereby stabilizing the beam against 'jitter' resulting from uneven accretion. If the accreted mass had an angular momentum direction different to that of the black hole, the radio source axis would swing appreciably on a time scale equal to the time it would take for the black hole to double its mass. If the postulated black hole in 3C196 is radiating at its Eddington luminosity, (see, for example, ref. 18) it must have a mass of at least $5 \times 10^7 M_\odot$ deduced from the radio power alone, and so to produce a rotation of the source axis on a time scale of $\sim 10^6 \text{ yr}$, the accretion rate would have to be at least $50 M_\odot \text{ yr}^{-1}$. The implied efficiency of conversion of accreted rest mass into relativistic particle energy leading to radio emission is $\sim 0.2\%$. The corresponding efficiency for 3C305 is $\sim 1\%$ assuming a rotation time scale of $5 \times 10^6 \text{ yr}$. If the efficiency of conversion of accreted rest mass into energy was as much as $\sim 30\%$ ¹⁹, the rotation time scale would be at least $\sim 10^8 \text{ yr}$, and the low efficiencies deduced here might create difficulties if 3C196, in particular, was found to be a strong X-ray or IR source.

In the case of 3C305, an alternative origin of the rotational symmetry is possible. The radio source is embedded in the galaxy, and if the axis of this source is not aligned with the rotation axis of the galaxy, then we might expect the galactic rotation to sweep energetic particles away from the compact hotspots in a rotationally symmetric fashion, thus producing the observed morphology. Sandage¹⁴ deduces a rotation period of $6.8 \times 10^7 \text{ yr}$ for the galaxy corresponding to a time scale of $\sim 2 \times 10^7 \text{ yr}$ for the degree of rotation observed here, and thus does not conflict with the lower limit of $\sim 5 \times 10^6 \text{ yr}$ deduced earlier.

The present observations strongly suggest that, in 3C196 and 3C305, the orientation of the source axis has rotated through a large angle over the source lifetime. Not only does the fact of source rotation place constraints on the source mechanism itself but its result is to separate spatially the radio emission generated at different stages in the source evolution. Future observations of such sources may thus provide valuable insights into the nature of radio sources in general.

We thank Drs D. Stannard and I.W.A. Browne for helpful discussions and comments. C.J.L. acknowledges an SRC research studentship.

Received 15 July; accepted 16 September 1980.

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MTRLI observations of the double QSO at 408 MHz

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The suggestion¹ that the twin QSOs 0957 + 561 A, B, which are separated by ~ 6 arc s and have emission redshifts 1.41, are images of a single QSO formed by a gravitational lens now seems to be generally accepted. This is a result of a wide range of data including optical spectroscopy^{2,3} and, more particularly, direct imaging by CCD camera⁴ and image-intensified photography (A. Stockton, personal communication) which reveal a galaxy, G1, with $m_r \sim 18.5$ within 1 arc s of the QSO B. G1 can account for the splitting of the images⁴. It is the brightest member of a cluster⁴, has a redshift 0.375 ± 0.005 (ref. 3) and IR observations confirm that it is a giant elliptical^{5,6}. The flux density ratio of the two QSO components is nearly constant, $B/A \approx 0.75$, from $\sim 3,000$ Å (ref. 7) to decimetre wavelengths^{8,9}, as expected for gravitational imaging. The first radio maps^{10,11} showed a complex structure and their initial interpretation was ambiguous, but there now seems to be agreement on the overall interpretation^{4,11,12} in terms of gravitational imaging. Early observations at 408 MHz (ref. 10) suggested the flux density ratio of the two QSO components may differ significantly from that at shorter wavelengths, which would cast doubt on the gravitational lens interpretation. Recent observations at 5 GHz (ref. 13) indicate a point source 1 arc s from QSO B, coinciding closely with the position of G1. We present here a 408-MHz map which provides spectral information on all components of the radio source, removes the doubt raised by the earlier 408 MHz observations and sheds light on the nature of the source coincident with G1.

0957 + 561 was observed at 408 MHz for 24 h on 8–9 January 1980 with the Jodrell Bank multi-telescope radio-linked interferometer (MTRLI)¹⁴ using four stations with six simultaneous independent baselines up to 127 km. Data were reduced by a CLEAN technique using closure phase and amplitude relations¹⁵, and restored with a synthesized beam of circular-gaussian shape with FWHM of 1.1 arc s. Using phase-closure relations means a loss of absolute positional information. Amplitude-closure relations were used to adjust gains of individual telescopes by amounts which in practice never exceeded 5%, and the resulting uncertainty contributed to the final flux scale is $\leq 2\%$. The flux scale was derived by reference to the compact source 3C119 which was assumed to have flux density 16 Jy. The peak of the resulting hybrid map (Fig. 1) is ~ 200 times the r.m.s. noise.

The 408-MHz map shows the general features of the map made with higher resolution (0.66×0.41 arc s FWHM) at 5 GHz (ref. 13). In Fig. 1 the component associated with QSO A is unresolved. Component B shows extension in a direction roughly that of G1, presumably due to the point source detected

at 5 GHz. The emission north-following A shows similar structure to that at 5 GHz; it has a steeper spectrum than A and accounts for more than two-thirds of the flux of the whole source. The emission south-preceding A is extended in a similar direction to that seen at 5 GHz and has a spectrum similar to that of the north-following emission.

The structure of the emission in the neighbourhood of component B was investigated as follows. Profiles through the peak of B were examined in the direction of G1 and the perpendicular direction; lower-level contours than shown in Fig. 1, extending down to the noise limit, were used for this. (The best estimate of the position of G1, 0.99 arc s N and 0.19 arc s E of QSO B, comes from the photograph by Stockton (personal communication) in seeing of half arc s.) The sections in the E–W direction and southwards from the peak showed no deviation from the point-source response down to the noise level, whereas the northern skirt showed a systematic broadening. Accordingly we assume that the contribution of QSO B is that of a point source at the position of the peak on the map. (This is supported by the fact that the peaks of A and B on the map are separated by 6.170 ± 0.005 arc s, in close agreement with the value of 6.175 arc s determined by VLBI⁸.) The flux density of B is 55 mJy. Subtraction of this point source leaves residual emission which is well represented by a point source of 3.3 ± 1.3 mJy at a distance 1.2 ± 0.2 arc s from B. This separation agrees well with the optical value quoted above for G1 and the 5 GHz value of 1.07 arc s (ref. 13).

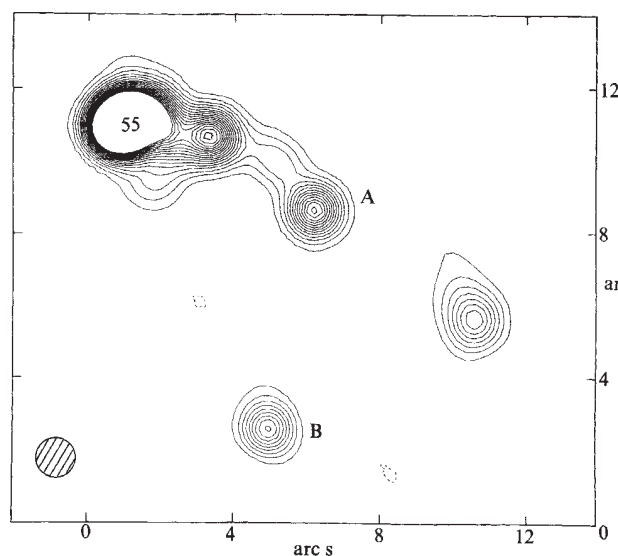


Fig. 1 Map of 0957 + 561 at 408 MHz. The zeros on both axes are arbitrary. The contour interval corresponds to a point source of 6 mJy; the zero contour is omitted, and negative contours are broken. The lowest contour is $\sim 4\sigma$. The half-power beam is indicated in the lower left corner.

The flux density of component A is 79 mJy. The ratio of flux densities, B/A is 0.70 ± 0.03 , where the standard deviation quoted is derived from the estimated noise on the map. This value is within the range of published flux density ratios at shorter wavelengths from radio to UV. It extends by a factor of more than three the longest wavelength at which the ratio is accurately determined and replaces the anomalous value obtained previously¹⁰ using single baselines of the present interferometer. There is evidence for variability of flux density at optical¹⁶ and radio¹³ wavelengths. Because sources generally vary less at 408 MHz than at higher frequencies, the new 408-MHz flux density ratio may be the most accurate value

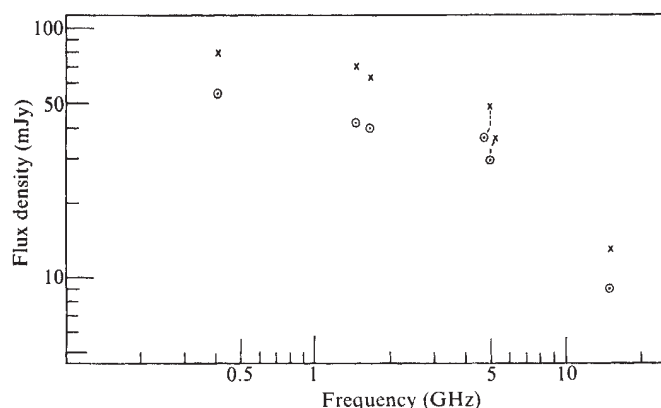


Fig. 2 Spectra of the compact components A (x) and B (o). 0.408 GHz, epoch January 1980 (this paper); 1.5 GHz, October 1980 (ref. 9); 1.67 GHz, February 1980 (ref. 17); 5.0 GHz (higher values), May 1979 (ref. 10); 5.0 GHz (lower values), February 1980 (ref. 13); 15 GHz, October 1979 (ref. 9).

available for the ratio inherent in the gravitational imaging process.

The radio spectra of A and B have now been determined over the range 0.408–15 GHz and are shown in Fig. 2, where the epochs of measurement are indicated. The values at 1,666 MHz are from VLBI observations using the European Network¹⁷ and supersede those published previously⁸. The disagreement between the two values at 5 GHz is unlikely to be due to variation as the values determined in May 1979 with the Cambridge 5-km telescope¹⁰ are considerably higher than the values determined with the VLA at three epochs^{11–13} June and October 1979 and February 1980; one or both measurements are likely to have systematic errors. The spectra show marked curvature with a high-frequency fall-off, although the extent of this is strongly dependent on the 15-GHz values⁹ which are only preliminary.

The weak component coincident with G1 may be emission from G1 itself or, more intriguingly, a third image of the QSO (or a combination of the two). Attention was drawn to the possibility of multiple imaging in the first published maps¹⁰ and more thorough calculations⁴ show a wide range of imaging geometries is possible, including ones giving rise to a third image close to the centre of G1. If the radio component is in fact a third image, its spectrum should be similar to that of A and B. We find the flux density ratio of B to this component is 16 ± 7 at 408 MHz whereas the value at 5 GHz (ref. 13) is 12.7 ± 1.1 . Thus it is possible that a third QSO image has been detected.

We thank our many colleagues at Jodrell Bank for the construction and operation of the MTRLI, and the development of data reduction techniques. We thank Dr Alan Stockton and Professor Bernard Burke for results before publication.

Received 1 August; accepted 12 September 1980.

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Magnetic domain observations of nucleation processes in fine particles of intermediate titanomagnetite

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The stable carriers of the palaeomagnetic record in rocks are commonly fine grains of magnetite or titanomagnetite ($\text{Fe}_{3-x}\text{Ti}_x\text{O}_4$) between 1 and 15 μm in diameter. The magnetic properties of these particles are therefore of interest to palaeomagnetists who must rely on them to preserve the Earth's magnetic field record over geological time. We report here domain observations of titanomagnetites in samples from Leg 49 of the Deep Sea Drilling Project. The results indicate that a major contributor to 'pseudosingle-domain' (PSD) saturation remanence is single domain remanence of particles larger than the classical single-domain threshold size which fail to nucleate domain walls in this magnetization state.

In contrast to larger, typically multidomain particles, the magnetic properties of titanomagnetites $\leq 15 \mu\text{m}$ are strongly grain-size dependent. Within this range, the coercivity H_c , the ratio J_{rs}/J_s of saturation remanence to saturation magnetization, and the low-field (<1 Oe) thermoremanent magnetization (TRM) acquired per unit volume of material increase roughly as $1/L$ (L is grain size)^{1,2} from nearly size-independent, multidomain values to their maxima at the single-domain boundary. The rapid rise of stability and remanence with decreasing grain size in particles still large enough to accommodate domain walls has led to their being referred to as 'pseudosingle-domain'³.

Stacey originally proposed that Barkhausen discreteness of domain wall position resulted in an intrinsic, undemagnetizable PSD moment³. It was later suggested⁴ that PSD moments arise within surface closure domains, or within a fine structure in domain walls which terminate at the surface. Domain wall moments have also been considered as a source of PSD remanence in sub-micrometre size magnetite by Dunlop⁵, who referred to such moments as 'psarks'.

These PSD models are based on the assumption that particles larger than the classical single-domain threshold size contain domain walls, regardless of their magnetization state. The role of nucleation—the process by which domain walls are initially formed—has not been considered in PSD models. Yet Becker^{6,7} has shown that the high coercivity of fine Co_5Sm particles is nucleation-controlled, and Banerjee⁸ noted that nucleation sites

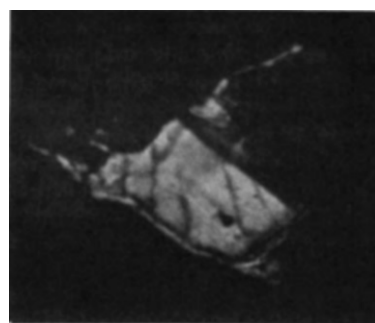
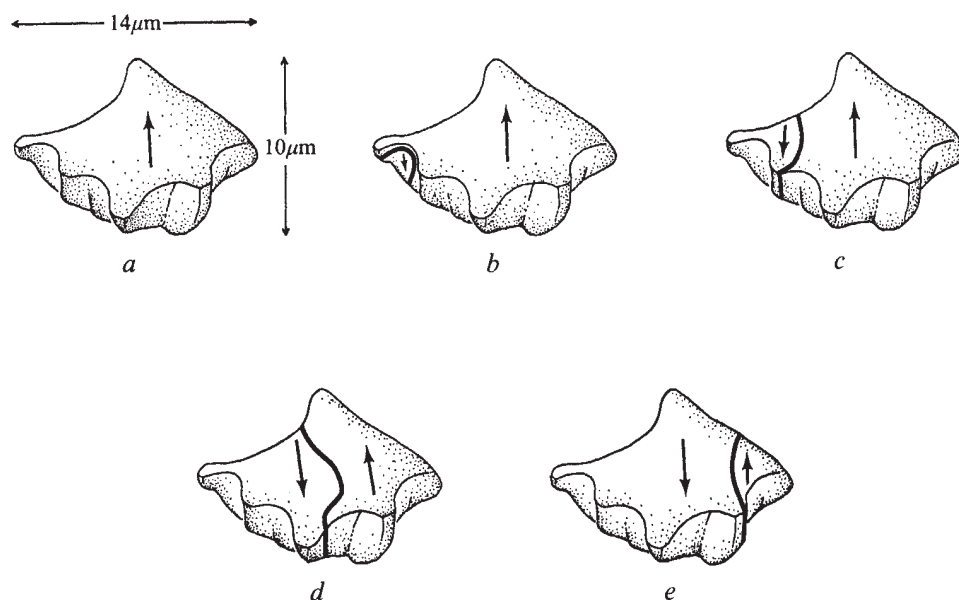


Fig. 1 Domain pattern on an ionically polished titanomagnetite particle, using the Bitter technique. Scale bar, 20 μm .

Fig. 2 Small titanomagnetite particle undergoing hysteresis in an applied field parallel to the magnetization: *a*, state of saturation remanence after reducing saturating field of 1,500 Oe to zero. Arrow indicates sense of domain magnetization, which is parallel to grain surface. *b*, Nucleation of small reverse domain in a reverse field of -12 Oe. Domain wall is indicated by heavy black line. *c*, $H = -30$ Oe. Note that this grain displays three-dimensional relief, and that the surface domain structure penetrates the grain volume. *d*, $H = -40$ Oe, *e*, $H = -48$ Oe.



may be the origin of high coercivity in fine-grained magnetite. The present domain observations strongly suggest that the nucleation process is important in determining the PSD properties of fine-grained titanomagnetite. These observations will be incorporated in a simple model which accounts for much of the grain-size dependence of J_{rs}/J_s in the PSD range.

Selected samples of oceanic basalt collected on Leg 49 of the DSDP were used for domain observations; their rock magnetic properties have been reported elsewhere⁹. The rocks chosen contain fresh titanomagnetite particles of composition $x = 0.6$. Specimens were first mechanically polished, and then ionically polished using the method of Soffel and Petersen¹⁰ to obtain the strain-free surfaces necessary for domain observation. The walls were observed with the Bitter technique (Fig. 1).

A small ($\approx 12 \mu\text{m}$) titanomagnetite particle undergoing hysteresis is shown in Fig. 2. The particle is initially saturated in a 1,500-Oe field. When the applied field is reduced to zero, the grain remains in the saturated state. On applying a 12-Oe reverse field, a small, reversely magnetized domain is nucleated. Further increase of the reverse field drives the wall towards the grain's interior, and magnetization reversal takes place by wall motion. The second half-cycle of hysteresis is identical to the first, except that the magnetization and field polarities are reversed.

Nucleation always occurs at the same location during each half-cycle, indicating that this grain utilizes only one nucleation site. As the polarity of the freshly nucleated reverse domain is always opposite to that of the saturating field, the grain has been truly saturated.

Similar behaviour has been observed in many particles of this size or smaller. In a population of 60 particles whose grain sizes are uniformly distributed between 5 and $15 \mu\text{m}$, 40% are observed to remain as single domains in saturation remanence, although one or more walls are subsequently nucleated in reverse fields. Another 40% of the grains contain two domains in saturation remanence, while the remainder contain three domains or more. It is also observed that grain size alone does not uniquely determine the saturation-remanent domain state, because particles of the same grain size exhibit a range of domain multiplicities.

These observations are consistent with the calculations of Brown¹¹. For a wall to nucleate, the spins must initially overcome an energy barrier originating in the various anisotropy energies. Brown's nucleation condition requires that $H_{ap} + H_d \geq 2K/J_s$, where H_{ap} is the applied field, H_d is the demagnetizing field, $2K/J_s$ is the anisotropy field, and where it is understood

that the sense of $H_{ap} + H_d$ is opposite to that of J_s . Particles of certain materials will, therefore, theoretically never develop domain structure in saturation remanence ('Brown's paradox')¹². However, there is considerable experimental evidence that nucleation occurs at surface imperfections at which there is either a strong, local demagnetizing field or an anomalously low anisotropy field^{6,13}. When a particle contains no nucleation sites which satisfy the above condition, it will remain as a single domain in saturation remanence, and will require a reverse field which aids H_d before domain walls appear. Such 'back-field' nucleation has been directly observed in iron whiskers¹³, in individual Co_2Sm particles⁶ and in the titanomagnetites described here.

If a sizeable percentage of grains fail to nucleate in saturation remanence, then these same particles will contribute significantly to the remanence of the assemblage. Moreover, the 'single-domain-like' fraction of a sized assemblage will increase as the mean grain size of the assemblage decreases, as the average number of nucleation sites per particle will decrease as the grain's surface area diminishes. The exact relationship between the number of sites and the number of walls is not understood, because the number of sites which actually succeed in nucleating will depend on the sites available as well as the number of domains which an individual particle can contain. However, we can still propose a simple model for the contribution to J_{rs}/J_s from particles which fail to nucleate in saturation remanence.

On the basis of the domain observations, it is first reasonable to assume that the nucleation sites are randomly distributed throughout a population of particles. Thus, the number of walls per particle in grains of a given size will vary probabilistically. Second, because nucleation sites vary in 'strength' according to whether or not the condition $H_d \geq 2K/J_s$ is fulfilled, it is likely that the fraction of sites which nucleate in J_{rs} is small ($\ll 1$). If nucleation can thus be defined to be a 'rare' event, then the number of walls per particle present in J_{rs} can be most simply described by a Poisson distribution.

Let w be the number of walls present in a grain of size L in J_{rs} , and let λ be the average number of walls, per particle, in J_{rs} . In general, λ will be a function of the grain size L . Therefore, the probability of there being w walls is

$$P(w) = \lambda^w e^{-\lambda} / w!$$

The contribution to J_{rs}/J_s from particles which do not nucleate in J_{rs} will be

$$J_{rs}(w=0)/J_{s,\text{total}} = e^{-\lambda} (j_{rs}/j_s)_{\text{SD}}$$

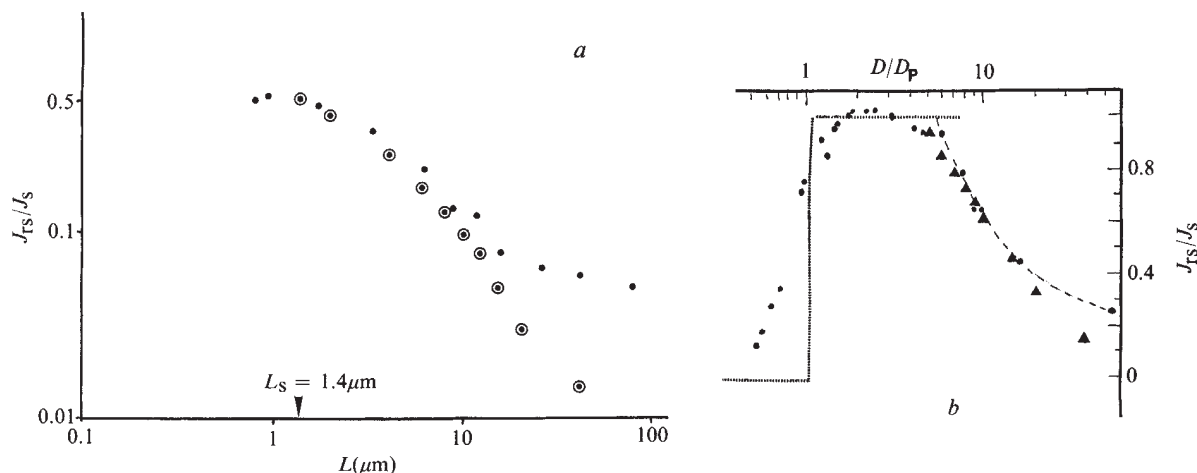


Fig. 3 *a*, J_{rs}/J_s versus grain size in randomly oriented $x = 0.6$ titanomagnetite. ●, Experimental data¹; ○, $P(w = 0)$ (j_{rs}/j_s)_{SD}. *b*, J_{rs}/J_s versus grain size in randomly oriented Co-Fe alloy at 76 K (ref. 16). Grain size is normalized to superparamagnetic size $D_p = 64$ Å; and $D_{SD} = 286$ Å (after ref. 16). ●, Experimental data; ▲, $P(w = 0)$ (j_{rs}/j_s)_{SD}.

where $(j_{rs}/j_s)_{SD}$ is the ratio of saturation remanence to saturation magnetization for single-domain particles of the material under consideration.

Once λ is known, then the single-domain-like contribution to J_{rs} may be calculated as a function of grain size. Ultimately, λ must be experimentally determined, but it is possible to set an upper limit for λ as follows.

Kittel¹⁴ predicted that the number of domains, n , contained by a cubic particle of length L should be

$$n = J_s(1.705L/\gamma)^{1/2}$$

where J_s is the spontaneous magnetization (G); γ , the specific wall energy (erg cm⁻²); and L the grain size (cm). This relationship has been verified for $x = 0.55$ titanomagnetite¹⁵. Because this calculation minimizes the sum of wall and demagnetizing energy without considering the magnetization state or nucleation difficulties, we will set $\lambda_{max} = J_s(1.705L/\gamma)^{1/2} - 1$.

The single-domain size $L_{SD} = \gamma/(1.705J_s^2)$ by the Kittel calculation, so that

$$J_{rs}(w = 0)_{min}/J_{s,total} = \exp[-(L/L_{SD})^{1/2} + 1](j_{rs}/j_s)_{SD}$$

This model therefore gives the minimum contribution to J_{rs}/J_s from the particles which fail to nucleate in an assemblage of identical particles with grain size L .

This model has been compared to J_{rs}/J_s in randomly oriented grains of $x = 0.6$ titanomagnetite, measured by Day¹. The single-domain size is estimated to be 1.4 μm, at which the experimental value of $J_{rs}/J_s = 0.5$. This estimate is consistent with that of Soffel for $x = 0.55$ titanomagnetite¹⁵. Figure 3*a* shows that there is good agreement between the model and the data in the PSD range. The model ceases to be important above 20 μm where the grains are truly multidomain.

In Fig. 3*b* the model has been compared to J_{rs}/J_s in randomly oriented Co-Fe alloy particles at 76 K, after Kneller and Luborsky¹⁶. J_{rs}/J_s is normalized with respect to the single-domain value of 0.46. Again, the model accounts for nearly all of J_{rs}/J_s in the PSD region which, for this material at 76 K, lies approximately between 300 and 1,300 Å.

The present domain observations indicate that, at least in $x = 0.6$ titanomagnetite, a major contribution to PSD saturation remanence is due to the single-domain remanence of particles which fail to nucleate domain walls in this magnetization state. The present model agrees well with the grain-size dependence of J_{rs}/J_s in two very different magnetic materials, thereby indicating that nearly all of the saturation remanence in the PSD range may be due to particles that do not nucleate walls in this state. The observations and the model suggest that the remanence stored by domain wall displacement is of minor importance in the PSD range, and is significant only when the particles are truly

multidomain. However, additional domain observations are in progress to test the validity and generality of the model, as well as its applicability to other aspects of PSD behaviour such as the size-dependence of coercivity and weak-field TRM.

We thank Professor Dr H. Soffel for details of his ionic polishing technique.

Received 14 April; accepted 12 September 1980.

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Implications for the primitive atmosphere of the oxidation state of Earth's upper mantle

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Knowledge of the oxidation state of the Earth's mantle is critical for understanding the processes of magma genesis and the composition of deep-seated volatiles. Measurements reported here of the intrinsic oxygen fugacities (f_{O_2} s) of mantle-derived spinels from peridotite and megacryst assemblages show that the Earth's upper mantle is close to the synthetic iron-wüstite (IW) buffer curve in f_{O_2} versus T space. It seems likely that most erupted volcanics are oxidized after their formation, perhaps by diffusive H_2 loss¹. There is a strong possibility that the mantle was in equilibrium with a core-forming metal phase, and that subsequent oxidation of the upper mantle resulted from an interaction between the present oxidizing atmosphere-hydrosphere and the mantle by subduction processes. Evidence in support of this mechanism has been supplied by rare-gas analyses of deep-seated nodules from kimberlites².

The gas species composing the early terrestrial atmosphere that formed through the degassing of the mantle having an oxygen state close to IW would have been profoundly different from those gases emitted from present-day volcanoes. The early primitive atmosphere would have been dominated by H_2 , CH_4 , CO and H_2S (that is reduced) rather than by the present-day, oxidized assemblage of H_2O , CO_2 and SO_2 .

It has generally been assumed that the abundance ratios of gases emitted by recent volcanic activity reflect equilibrium with the sources of erupted magmas³, and that these relative abundances have remained essentially unchanged through geological time⁴⁻⁶. These assumptions have led to the supposition that the oxidation state of the Earth's upper mantle is, and always has been, close to the f_{O_2} defined by the quartz-fayalite-magnetite (QFM) buffer at any given temperature^{7,8}.

Oxygen ion-specific properties of stabilized, solid ZrO_2 electrodes^{1,9} can be used to measure the oxidation state of mantle-derived materials directly. By modifying the published techniques⁹ we have improved the precision, accuracy and reversibility of ZrO_2 cell signals obtained^{10,11}. Our approach involves isolating the e.m.f. signal generated by the sample from that unavoidably imposed by the residual atmosphere inside the sample-bearing cell. By varying the f_{O_2} of the residual atmosphere inside the cell, it is possible to determine a 'plateau' value of constant f_{O_2} relative to an external furnace atmosphere which represents a reversed, intrinsic f_{O_2} measurement for the sample alone. The extent of the plateau reflects the innate O_2 -buffering capacity of the sample relative to the residual atmosphere. All previous measurements of intrinsic f_{O_2} s of geological samples have failed to achieve true reversals of the cell signals, and the published data^{1,9,12-14} must represent upper, oxidized limits to the true values.

Our techniques have been used to measure the intrinsic f_{O_2} of spinels from peridotite and megacryst assemblages from Victoria (Australia), Arizona (US) and West Germany. These peridotite samples are considered to be representative of portions of the upper mantle in the pressure range ≈ 20 – 25 kbar, whereas the spinel megacrysts are believed to be high-pressure (≥ 10 kbar) equilibrium cumulates from basaltic magmas^{15,16}. The major element compositions of the peridotites are similar to samples from the same region of Victoria and Dreiser Weiher described by Frey *et al.*¹⁷ and Jagoutz *et al.*¹⁸ as somewhat depleted in basaltic components.

The intrinsic oxidation states relative to the IW buffer range from $\approx 0.25 \log_{10} f_{O_2}$ units more oxidized to 1 $\log_{10} f_{O_2}$ unit more reduced (Fig. 1). The overall reduced nature of the spinels, as well as the considerable range of f_{O_2} s obtained, are striking features of the data. We note that recent electrochemical cell data obtained by Ulmer *et al.*¹² on upper mantle-derived olivines plot close to the IW buffer, but the true values must be more reduced than that in view of the experimental technique. Figure 1 also shows f_{O_2} plotted against T for common basic eruptive rocks determined from analysis of coexisting Fe–Ti oxide minerals¹⁹. The difference of $\sim 4 \log_{10} f_{O_2}$ units between the oxidation states of peridotites and igneous rocks may be due to late-stage oxidation of the latter, perhaps by H_2 loss¹. Alternatively the generation of magma in the upper mantle might involve a precursor, metasomatizing event^{20,21} that causes localized oxidation and lowering of solidus temperatures relative to the bulk of the mantle. Limited data on the intrinsic f_{O_2} of kimberlite²² suggest that some mantle-derived magmas may be as oxidized as values of f_{O_2} equivalent to QFM. In general, however, the proposed mechanism of H_2 loss by magmas at shallow depths within the Earth is the favoured explanation for the contrast in oxidation states of erupted and deep-seated rocks due to the highly reduced nature of the spinel megacrysts from Arizona, and a deep-sea Hawaiian basalt¹ (Fig. 1).

We have noted^{10,11} that the intrinsic f_{O_2} of a spinel peridotite sample from Australia is only $\approx 2 \log_{10} f_{O_2}$ units more oxidized than that required for saturation with a potential core-forming Fe–Ni alloy. If oxygen is the main contributor towards lowering of the mean atomic weight of the Earth's core²³, rather than S

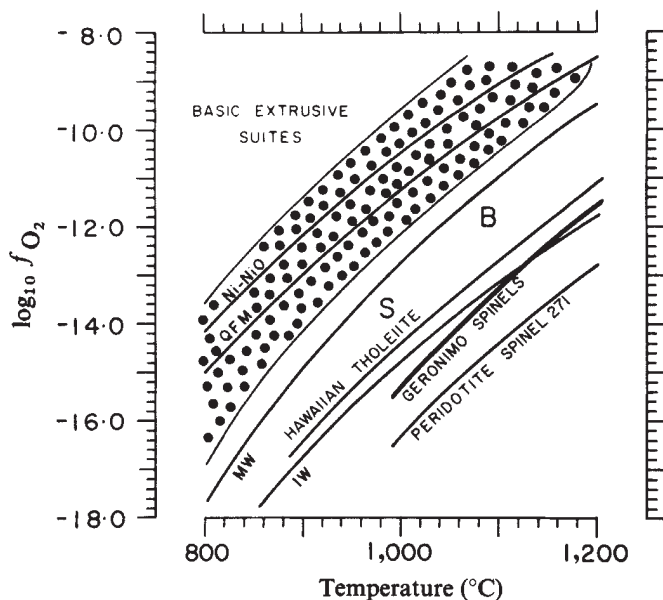


Fig. 1 f_{O_2} versus T data for common basic eruptive rocks compared with electrochemical cell determinations of intrinsic f_{O_2} s for plutonic and one volcanic rock. The dots outline the area of T versus f_{O_2} space in which $>95\%$ of the available data for basic volcanic rocks fall⁷. S and B represent the intrinsic f_{O_2} s and T s recorded for specific horizons in the Stillwater⁹ and Bushveld¹³ intrusions. The line for the Hawaiian tholeiite is data obtained by Sato⁹ for a submarine basalt on the flanks of Kilauea. Given the experimental techniques used for S, B and the Hawaiian tholeiite, these earlier data must represent the upper (oxidized) limits of the true intrinsic f_{O_2} s of the samples. Our data for one spinel peridotite from West Germany fall very close to the curve for Hawaiian tholeiite. Geronimo spinels are megacryst samples from Arizona while spinel 271 is from Victoria, Australia. Buffers: MW, magnetite-wüstite; Ni–NiO, nickel–nickel oxide; IW, iron–wüstite; QFM, quartz–fayalite–magnetite.

(ref. 24) or Si (ref. 25), then the values of intrinsic f_{O_2} reported here for portions of the Earth's upper mantle must be even closer to those required for equilibrium with the core. During the separation of a core-forming metal phase from the proto-mantle, an equilibrium of the sort described by



would buffer the f_{O_2} of the system, at least at low pressures (<100 kbar). At higher pressures, phases other than orthopyroxene and olivine would be involved and the disproportionation of Fe^{2+} to Fe^{3+} and Fe metal would be a significant redox control²⁶.

The variation in f_{O_2} s for mantle-derived samples collected from widely separated locations on the Earth could be due either to (1) the persistence of primary accretional heterogeneities in the Earth that have lasted for 4,600 Myr or (2) localized oxidation of the mantle following the onset of plate-tectonics.

The development of subduction as a major terrestrial tectonic feature raises the possibility that volatiles (for example, seawater bound in hydrous minerals, CO_2 in carbonates) and oxidized oceanic crust can be transported into the upper mantle causing a progressive and irreversible oxidation of the Earth's upper mantle, especially at shallow levels. While no consensus has emerged in the petrological debate over the involvement of the subducted slab as a source of volatiles and magmas at island arcs and collisional continental margins²⁷⁻²⁹, there is no doubt that devolatilization of the subducted slab must occur especially at pressures <25 kbar (refs 30, 31). Because the upper layers of the subducted lithosphere reflect prolonged interaction with the atmosphere–biosphere–hydrosphere system, which is dramatically oxidized relative to the f_{O_2} s prevailing in the upper

mantle, contamination of the mantle by a subducted component is a plausible oxidation mechanism over geological time.

Since the studies of Rubey³² and Holland³³ on the evolution of the atmosphere and hydrosphere, it has been assumed³ that the present-day volcano-associated gas abundances constrain the oxidation state of the upper mantle to that equivalent to the QFM buffer. This assumption, together with the supposed overabundance of siderophile elements in the upper mantle³, have led to conclusions that the mantle was never in equilibrium with a core-forming metallic phase. We have proposed³⁴ that the relatively high abundances of siderophile elements in the mantle (for example, Ni, Co, Pt group metals, W, Mo, Sn, Ag, Sb, Cu) can be explained by a combination of early equilibrium between a metal-silicate-sulphide system, and incomplete separation of sulphide into the core-forming metal, followed by meteoritic contamination³⁵ after core separation ($\approx 4,500$ Myr). As at low f_{O_2} s and relatively high f_{S_2} , a significant proportion of the siderophile elements are partitioned into the sulphide phase, the supposed overabundance of siderophile elements in the mantle does not negate the possibility of core-mantle equilibrium.

Assuming a mantle close to the IW buffer in terms of oxidation state, it is possible to compute the nature of the gas species in the system C-O-H-S that would be in equilibrium with Fe-Mg silicates and oxides³⁶⁻³⁸. If the Earth's interior was an effectively closed system with respect to gaseous constituents during the earliest stages of planetary differentiation, then the volatile species residing in the mantle after core formation would have been in chemical equilibrium with the core-mantle system. In these conditions, gas-species computations show that CH₄, H₂, H₂S and CO become volumetrically significant with respect to H₂O, CO₂ and SO₂ (refs 36-38). Although the latter species may remain collectively the most abundant, it is important to note that condensation and low-temperature, selective reaction of the primitive crust with H₂O, CO₂ and SO₂ could have resulted in a strongly reducing primitive atmosphere composed of CH₄, NH₃, H₂, CO and H₂S with lesser amounts of H₂O vapour and CO₂. Diffusive loss of H₂ from the atmosphere³⁹, together with the evolution of life that was initially promoted in this reducing environment⁴⁰, has ultimately resulted in a progressive oxidation and alteration of the primitive atmosphere⁶.

We propose that during partial melting of the upper mantle to produce basaltic magmas, the intrinsic f_{O_2} prevailing in the melt-residue system is close to the IW buffer. However, as these magmas rise towards the Earth's surface, their systems become open by H₂-loss and interaction with the oxidized crust-hydrosphere-atmosphere resulting in oxidation levels in the vicinity of QFM. This is generally supported by the observation that magmatic systems are dominated by low-pressure equilibria⁴¹. While the oxidation state of the Earth's upper mantle is presently not in equilibrium with a metallic phase (the core), probably due to its contamination by oxidized, subducted components, it is significantly more reduced than the erupted magmas. Finally, our results on the intrinsic f_{O_2} of the Earth's upper mantle support the view that the early terrestrial atmosphere, which is known to have been formed by degassing of the Earth's interior, was strongly reducing relative to the present atmosphere and volcanic gases.

Received 16 June; accepted 28 August 1980.

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Variations of ground radon concentrations with activity of Kilauea Volcano, Hawaii

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Measurements of the concentration of the radioactive gas radon, in particular relative areal variations in Rn outgassing (mainly isotopes ²²²Rn, $t_{1/2} = 3.82$ days and ²²⁰Rn, $t_{1/2} = 54.5$ s), at shallow ground depths (30 cm) are being used extensively in Hawaii in the exploration for geothermal resources^{1,2}. Zones showing a greater than usual degree of Rn ground gas outgassing have delineated areas of anomalous subsurface heat and increased permeability. The patterns of outgassing suggest that thermally induced ground gas convection systems have developed¹. Nine measurement stations have been established on the upper east rift of Kilauea volcano along the Chain of Craters Road (Fig. 1) to observe: (1) temporal variations in Rn outgassing; (2) relationship between Rn outgassing and variations in seismicity; and (3) whether this technique can assist in understanding the 'plumbing' of Kilauea and whether monitoring of a larger number of stations could assist in indicating pre-eruptive activity. These nine stations, initially included in a summit-wide survey (August-September 1978), were re-established in October 1979 because of the increased seismic activity within the upper east rift. Fortunately, a small eruption of Pauahi Crater occurred on 16-17 November 1979 at the end of the first one-month period of measurement. The present results indicate that the Rn concentration increases before and during seismic events, then decreases before returning to a 'normal' value.

Variations of Rn concentration associated with changes in the activity of volcanoes and volcanically-induced earthquakes are most commonly reported from measurements of hot spring waters and fumarolic or spring gases³⁻⁶. These Rn values often have large fluctuations that cannot always be correlated with variations in volcanic or seismic activity. Rn measured in groundwaters on Karymsky volcano has, however, shown such correlation⁷ and in Hawaii, widely spaced measurements on Kilauea's summit and east rift indicated increased ground Rn outgassing during periods of increased seismic activity associated with the September 1977 eruption of Kilauea⁸.

In the current survey, the concentrations of Rn in ground gas were measured by using α particle-sensitive films (Kodak, LR 115, II) that were field exposed for periods of three to four

weeks^{1,9,10}. To distinguish between the Rn contribution from soil immediately below the measuring device and Rn derived from a greater depth and transported by convection, the Rn emanation was measured in the laboratory by using one sample of soil from each station, and then was subtracted from the total measurement^{1,11}. The Rn concentration units are α tracks (T) $\times 10^{-2} \text{ cm}^{-2} \text{ h}^{-1}$ (1 unit $\approx 1.03 \times 10^{-4} \text{ nCi l}^{-1}$). The Rn emanation from the soil samples (all derived from tholeiitic basalt lavas) ranged from 0.5 to $2.15 T \times 10^{-2} \text{ cm}^{-2} \text{ h}^{-1}$. Duplicate laboratory measurements of Rn emanation from five different soil samples had a mean precision of $\pm 3.5\%$. Quadruplicate measurements in the field at one location gave a mean observed variation in corrected values of 10%. When these corrected field-measured concentrations at a station were lower than the Rn emanation from the soil at that location, the Rn concentrations are reported as negative values. Negative or very low positive values suggest that the flow of ground gas at that site is downward or, in some cases, static.

Areal variations in concentration measured during the summit-wide survey of Kilauea suggest that the long-term pattern on the summit is of strong outgassing within the caldera and associated major fractures, with a net downflow of ground gas in the peripheral area and on the upper flanks of Kilauea. This net downflow is, however, variable and responds to localized events such as described here, as well as being affected by the existence and location of faults and fractures that enable strong upflows to occur. The development of similar, but linear and areally restricted convection systems has also been observed over rift zones in Hawaii¹.

The data for August 1978 were collected during a period of slow inflation in the Kilauea summit region¹². This buildup of activity followed a flank eruption in the central east rift in September 1977. The Pauahi eruption of 16–17 November 1979 was a minor eruption that lasted ~ 22 h and produced only a small volume of tholeiitic lava ($\approx 700,000 \text{ m}^3$) at relatively low temperatures¹² ($1,040$ – $1,080^\circ \text{C}$). Radon outgassing at the nine stations during August–September 1978 produced low positive values (Fig. 2). For the month up to and including the November 1979 eruption, values of Rn outgassing increased from 0.5 to 20.5 times the August–September 1978 measurements at seven of the nine stations (Fig. 2). The highest concentration was

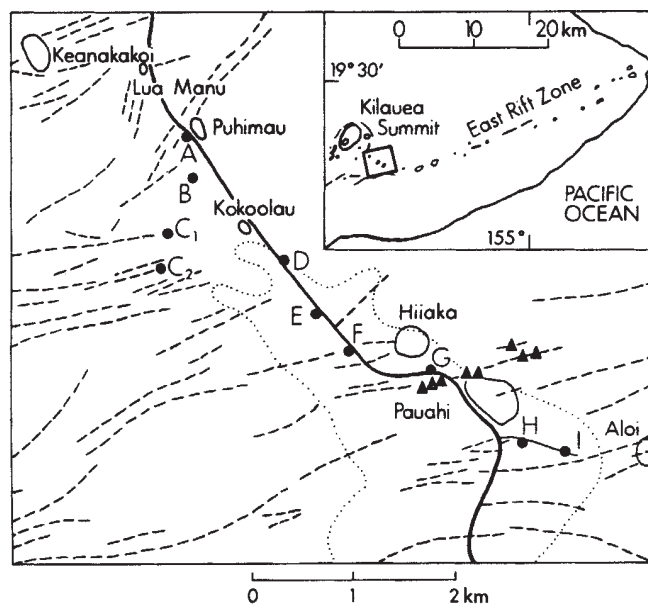


Fig. 1 Survey area. The inset shows the location of the survey area on the island of Hawaii, and solid lines show the craters and the Chain of Craters Road; ●, measurement locations; ▲, vents of November 1979 Pauahi eruption; broken lines show faults and major fractures; small dots show the outline of the area of concentration of shallow epicentres (1–5 km) preceding the eruption¹².

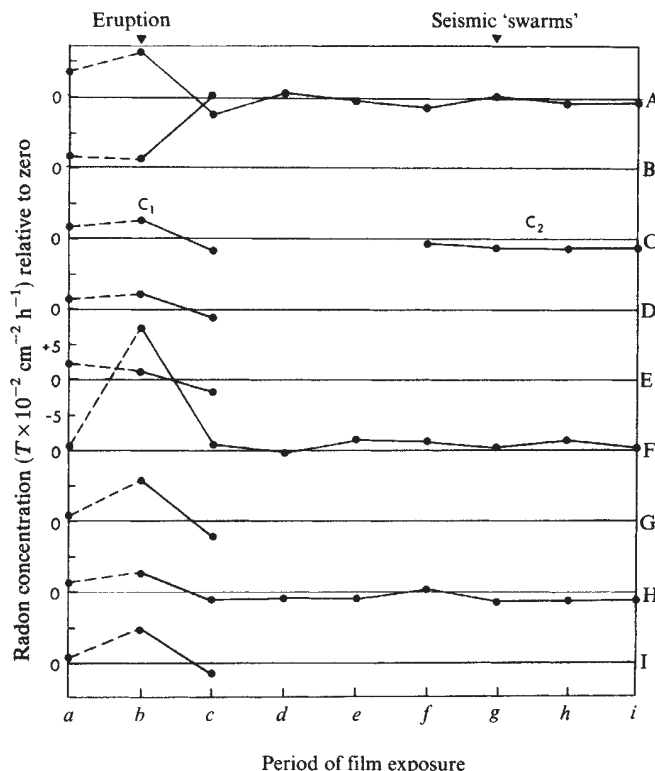


Fig. 2 Plot of Rn concentration at each station; each point is the value measured over an approximately four-week period and normalized to exposure time and surface area of film. The mean precision of the measurements was determined by field experiments to be $\pm 5\%$. a, 4 August–3 September 1978; b, 27 October–17 November 1979; c, 17 November–19 December 1979; d, 19 December 1979–15 January 1980; e, 15 January–6 February 1980; f, 6 February–27 February 1980; g, 27 February–20 March 1980; h, 20 March–10 April 1980; i, 10 April–3 May 1980.

recorded at Station F, next to an eruptive fissure that was active during the eruption of Hiiaka Crater in 1973. Rn outgassing was also high from a fracture associated with Puhimau Crater. This fracture extends to an area of steaming ground (between B and C), related to an intrusive event that occurred in 1938. At Stations B and E, Rn concentration before and during the eruption was 0.11 and 0.41 lower, respectively, than in August–September 1978. In the month following the Pauahi eruption, Rn concentration decreased significantly, mostly to negative values, at eight stations, and increased only at B. Stations A, F and H were monitored over the subsequent six months, and Station C was relocated and monitored over three months. During this latter period two episodes of seismic 'swarms' were significant. The first (2 March 1980) was located near Pauahi Crater, and the second (a week later) began in the same area and migrated ~ 6 km eastwards (D. M. Moore, personal communication); these seismic events were probably caused by intrusive activity. At this time the summit was experiencing its fourth week of deflation.

Smaller changes in Rn concentration occurred in association with the seismic swarms. At Station H, the closest to the activity, the Rn concentration increased during the month before the events and decreased after them. (Note that this seismic activity occurred in the first part of the measurement period 27 February–20 March 1980). At Station F, the Rn concentration gradually decreased before and during these events, behaviour which was inverse to that at H and which is considered to be a result of localized convective ground gas flow related to the activity below Pauahi Crater. At Station C₂, Rn concentrations remained much the same, but at A, concentrations increased to positive values during and immediately after these events, and then returned to negative values. This change is not fully

understood but could demonstrate some delay effect from the activity below Pauahi or possibly localized activity in the vicinity of Station A. Overall, Rn outgassing at three of the four stations underwent changes during the period of these seismic events, and subsequently returned to values apparently characteristic for each station.

We attribute the increases in outgassing associated with the eruption and the seismic events to various causes related to the movement of magma towards the surface and the associated deformation of the country rock. The rise of magma causes local temperature increases within the volcano and increases the fracture permeability. These conditions seem to permit Rn directly volatilized from the magma at high temperature to migrate towards the surface, transported by the escaping steam^{6,13,14}. This steam and the overall thermally stimulated, increased outgassing act as a transport medium for other available Rn encountered during migration towards the surface^{1,7}. The major sources of this additional Rn are the groundwater through which the vapour phases pass (Rn is more soluble in the vapour) and Rn within pore spaces and fractures in lava above the water table. A further source may be the decay of Ra within secondary mineralization (largely CaSO₄) deposited on fracture surfaces in zones where hydrothermal activity has occurred^{1,15}. Availability of minor quantities of Rn is possibly also enhanced by stress buildup and deformation, causing a greater diffusion of Rn by destruction of crystalline lattices of minerals and a greater pore space-transporting fluid area in contact at depth.

The common decrease in Rn concentration following the eruption and seismic swarms seems to be caused by depletion of Rn available in rock fractures and pores from 'flushing' by increased outgassing before and during these events. The Rn regenerates by decay of Ra and by diffusion into rock fractures over a period of several weeks, allowing an overall return to levels characteristic of periods of normal seismicity (no specific events). Similar post-eruptive Rn depletion was observed in thermal springs on Karymsky volcano⁴ and has been proposed as creating ²²⁶Ra-²²²Rn disequilibrium in pumice ejected during eruptions of Japanese volcanoes¹⁶. In both cases, a subsequent period of buildup was observed. In the case of ground Rn outgassing associated with an eruption, the post-eruptive reduction of near-surface heat and stresses at depth, partially decrease fracture permeability and allow the re-establishment of groundwater flow and consequent dissolution of much of the Rn being generated below the normal water table. After equilibrium conditions are again established, the greatest source of Rn to the surface is probably from the lava pile above the water table. The most important change, however, seems to be a reduction of thermally induced ground gas outgassing, which allows re-establishment of ground gas flow patterns. The greatest changes in outgassing were measured at stations close to fractures or faults below which there was magma migration, or other phenomena that produced increased seismic activity. Where Rn values at a station are atypical relative to adjacent stations (for example, B), they are apparently a consequence of localized ground gas convection systems developed around or between fractures. The flow of ground gas (whether upflow or downflow) in these systems is increased during these events, and in some cases, reversals in ground gas flow can occur usually within specific zones of fracturing.

Due to the apparent success of this study 25 stations (including the above) are now being monitored on the summit and along the east rift of Kilauea. The results from these stations reinforce the above findings, specifically, that the Rn concentration increases before and during seismic events (caused by either extrusive, intrusive, or earthquake activity) and decreases over several weeks after the event, then tends to return to a normal or characteristic value for each station. Atypical variations at some stations are indicated to result from location of fractures relative to each other and to the location of the event. Continuous monitoring of the larger number of stations will aid understanding of the fracture systems and the ground gas flow

patterns on the volcano, and may assist in indicating pre-eruptive activity.

We thank J. J. Naughton and D. B. Jackson for reviews and the staff of the Hawaii Volcano Observatory for cooperation. The study was carried out under US Department of Energy Contract no. EW-78-S-07-0713.

Received 29 April; accepted 19 August 1980.

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Trophic structure of a grassland insect community

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The idea that there is some underlying trophic structure to ecological communities has long been attractive¹⁻³. Energy, biomass or nutrients are undeniably transferred from one trophic level to another. However, does the number of species at one trophic level place constraints on the number of species at another trophic level? Cohen⁴ has shown that, in a sample of 14 community food webs, the ratio of prey species to predator species remains virtually constant. In an analysis of a grassland insect community, Evans and Murdoch⁵ have shown that the ratio of herbivorous insects to entomophagous insects remains fairly constant throughout the growing season. They speculated that this reflects an underlying trophic pattern that persists in the face of a continuing turnover of species. I have now found that a close examination of this pattern shows that an appearance of constancy can be generated by replicate samples taken from the pool of all available species.

The number of species of herbivorous and entomophagous insects in each sample interval may be envisioned as a random draw of species from the total pool of available species. In this case the number of herbivorous species would be a function of the total number of species drawn from the pool and the proportion of herbivorous species present in the species pool. The number of herbivorous species will have a hypergeometric distribution

$$P(k) = \frac{\binom{n}{n_1} \binom{n-n_1}{r-k}}{\binom{n}{r}} \quad (1)$$

Equation (1) gives the probability that exactly k herbivorous species will be found in a sample of r species taken from a total pool of n species of which n_1 are herbivorous species. The expected number of herbivorous species in a sample of size r is given by

$$E(H) = r \left(\frac{n_1}{n} \right) \quad (2)$$

The variance of this expectation is given by

$$\text{Var}(H) = r \left(\frac{n_1}{n} \right) \left(1 - \frac{n_1}{n} \right) \left(1 - \frac{r-1}{n-1} \right) \quad (3)$$

Table 1 The observed and expected numbers of herbivores in a grassland insect community

Fortnightly interval	No. of species	Observed no. of herbivores	Expected no. of herbivores	Expected variance in herbivore no.
1	20	12	12.4	4.4
2	32	22	19.9	6.6
3	64	40	39.7	10.8
4	92	62	57.1	12.6
5	116	77	72.0	12.7
6	137	88	85.1	11.7
7	147	98	91.3	10.8
8	150	95	93.2	10.5
9	133	79	82.6	12.0
10	144	91	89.4	11.1
11	127	78	78.9	12.3
12	98	64	60.9	12.8
13	52	29	32.3	9.5
14	22	18	13.7	4.8

The data from the 14 sample intervals of Evans and Murdoch specify all quantities of equations (2) and (3). The number of species is the quantity r . Other quantities are given in the text. The fit of observed values to theoretical expectations is tested by a $\chi^2 = 3.45$, d.f. = 13, $P > 0.995$.

The data from the 14 fortnightly intervals given by Evans and Murdoch are shown in Table 1. The total number of herbivorous and entomophagous species in this grassland community is given as 131 and 80, respectively. This represents values of $n = 211$ and $n_1 = 131$. All values of equations (2) and (3) are known and thus the expected number of herbivores and the expected variance can be calculated.

Figure 1 shows the observed number of herbivores and the expected number of herbivores. Points fall on the line if the expected number of herbivores equals the observed number. The bars through the points are 2 s.d. from the expected values. All but one of the points (fortnightly interval 7) lie within 2 s.d. of the expected value.

There seems to be no systematic tendency in the samples to lie either above or below the line. Four samples are found to have more herbivores than expected, 10 have fewer than expected. The two-tailed binomial probability for this, or a more deviant event, is $P = 0.284$.

There does not seem to be any trend in deviation from the expected as one considers various numbers of species. Two of the four values greater than expectations are above the median of total species, two of the values are below the median. When there are few species, at either the beginning or end of the

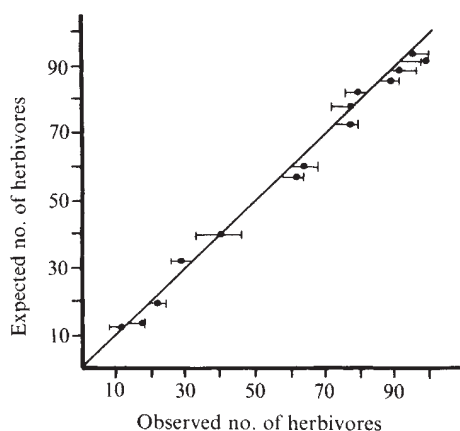


Fig. 1 The expected number of herbivores is plotted against the observed number of herbivores. The bars represent 2 s.d. from the expected number of herbivores.

season, there does not seem to be any less trophic structure. Nor does there seem to be more trophic structure during the period of greatest species diversity.

In conclusion, there does not seem to be any evidence that the ratio of herbivores to predators in this grassland insect community is maintained at a constant level by any other force than a statistical one. Analysis at another, deeper, level, well beyond the scope of this report, might ask why the ratio of herbivorous insects to their predators is 1.64. Given that it is, however, no further evidence for trophic structuring exists.

Received 2 June; accepted 10 September 1980.

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Co-transfer of determinants for hydrogenase activity and nodulation ability in *Rhizobium leguminosarum*

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In all organisms that fix atmospheric nitrogen a by-product of the nitrogenase reaction is hydrogen gas¹ which may dissipate up to one-third of the energy flux through nitrogenase². Some nitrogen-fixing bacteria, including certain strains of the root nodule bacterium *Rhizobium*, possess an active hydrogen uptake (Hup) system permitting hydrogen to be re-cycled^{3,4}. For this reason Hup⁺ *Rhizobium* strains are thought to be more energy-efficient symbionts than their Hup⁻ counterparts⁵⁻⁸. We report here that determinants for hydrogenase activity (*hup*) in a particular strain of *R. leguminosarum* (128C53) are genetically linked to determinants for nodulation ability (*nod*), and are probably carried on a plasmid, pRL6JI, of molecular weight (MW) ~19 × 10⁷. Although pRL6JI was not self-transmissible, the determinants for nodulation ability and hydrogenase activity (*hup*) could be transferred to other strains of *R. leguminosarum* after recombination with a derivative of a transmissible *R. leguminosarum* plasmid.

Nodulation ability is plasmid-determined in *R. leguminosarum*⁹⁻¹² and several determinants for nodule formation and function may be carried on a single plasmid¹¹⁻¹⁵. We therefore attempted to transfer determinants for nodulation ability from strain 128C53, a Hup⁺ field isolate of *R. leguminosarum*^{8,16}, into a non-nodulating (Nod⁻) mutant of the Hup⁻ field-isolate *R. leguminosarum* strain 300 in the hope that determinants for Nod⁺ and Hup⁺ were genetically linked and might consequently be co-transferred. The recipient strain was 16015, a derivative of strain 300, which contains *str-37* and *spc-54* markers and a plasmid deletion in a region determining nodule formation (Nod⁻) and nodule function (Fix⁺)¹¹⁻¹³.

Strain 128C53 contains two large plasmids (MW ~19 and 23 × 10⁷) but no evidence for self-transmissible plasmids was obtained using methods which had identified such plasmids in other *Rhizobium* strains^{9,14,17}. Therefore two self-transmissible plasmids, which did not themselves suppress the Nod⁻ phenotype of strain 16015 but which were known to mobilize nodulation plasmids from other strains¹³, were introduced into strain 128C53. The transmissible plasmids used were pVW3JI and pVW5JI, kanamycin-resistant derivatives of pRL3JI and pRL4JI respectively¹³.

Table 1 Co-transfer of Nod⁺ and Hup⁺ determinants from derivatives of strain 128C53 to strain 16015 following recombination with transmissible plasmids determining kanamycin resistance

Donor strain	Plasmid from which <i>kan</i> marker was derived	Recipient strain	Frequency of transfer of <i>kan</i> per recipient	No. of Kan ^r transconjugant clones tested on plants			
				Total	Nod ⁺	Fix ⁺	Hup ⁺
<i>a</i>							
2515	pVW3JI	128C53	2×10^{-4}	5	5	5	5
2517	pVW5JI	128C53	1×10^{-4}	5	5	5	5
<i>b</i>							
3856	pVW3JI	16015	5×10^{-7}	15	11	11	11
3957	pVW5JI	16015	5×10^{-7}	15	10	10	10
<i>c</i>							
2515	pVW3JI	16015	3×10^{-2}	10	0	—	—
2517	pVW5JI	16015	5×10^{-2}	10	0	—	—

a, Introduction of transmissible plasmids into 128C53 derivatives; *b*, transfer of plasmid-linked determinants from 128C53 derivatives to the non-nodulating strain 16015; *c*, control crosses: direct transfer of plasmids from 300 derivatives to strain 16015. Two derivatives of strain 300, each carrying a different transmissible plasmid conferring kanamycin resistance, were mated with strain 3854, a spontaneous *rif* mutant of strain 128C53 (itself a Hup⁺ field isolate of *R. leguminosarum*). The genotypes of the donor strains were as follows:— 2515:300 *phe-1 ade-27 rif-45* pVW3JI; 2517:300 *phe-1 ade-27 rif-45* pVW5JI. Kanamycin-resistant derivatives of 3854 (128C53 *rif-397*) were obtained by introducing pVW3JI or pVW5JI into this strain and these derivatives were termed 3856, 3957 respectively (*a*). These two strains, together with the corresponding strain 300 donors were used in crosses to the Nod[−] strain 16015 (*b* and *c*). Kan^r derivatives of 16015 were repurified and scored for nodulation ability on duplicate peas, var. Wisconsin Perfection. Roots of nodulated plants were tested for acetylene reduction (Fix⁺) and for the incorporation of tritiated hydrogen gas (Hup⁺) into the aqueous phase as described in Table 2.

When the 128C53 derivatives into which pVW3JI or pVW5JI had been introduced were used as donors to strain 16015, transfer of *kan* occurred at low frequency (10^{-6} to 10^{-7} per recipient). However, more than half of the 16015 transconjugant clones were now able to nodulate peas (Table 1). In all cases the nodules formed had hydrogenase activity comparable to that for strain 128C53 and the rate of hydrogen evolution was correspondingly diminished compared with a Hup[−] strain (Table 2).

Because strain 300 itself is Hup[−] and neither Nod⁺ nor Hup⁺ phenotypes are conferred by pVW3JI or pVW5JI (data not shown), both Nod⁺ and Hup⁺ determinants must have been derived from strain 128C53 and must therefore be genetically linked in that strain. This was confirmed in further crosses between the 16015 Kan^r Nod⁺ Hup⁺ transconjugants and strain 6015 (which carries the same *nod-6007* deletion as strain 16015²): in these crosses *kan* was transferred at high frequency (5×10^{-3} per recipient) and most (22/25) of the Kan^r 6015 transconjugants were also Nod⁺. In all cases Nod⁺ transconjugants were Hup⁺. The very high-frequency co-transfer of *nod* and *hup* with *kan* suggests that there has been genetic recombination between these markers, and the high-frequency transfer of *kan* suggests the involvement of a plasmid, at least at this stage.

The transfer frequency of *kan* from the 128C53 derivatives to strain 16015 was inexplicably low but was at least 10-fold higher than for transfer of chromosomal alleles (data not shown). When similar crosses were performed using the P1 group R plasmid pJB3JI (which confers tetracycline resistance¹⁴), the Tet^r determinant was transferred into and out of strain 128C53 at normal frequencies (10^{-2} – 10^{-3}), but no co-transfer of Nod⁺ to strain 16015 was observed (data not shown).

Because the Nod⁺ determinants of strain 128C53 were probably plasmid-borne, the plasmids from many of the strains described here were examined after electrophoresis on agarose gels (Fig. 1). In strain 2515, a 300 derivative, the plasmid pVW3JI was visible as the second-fastest migrating band, MW 13×10^7 (Fig. 1 track *a*, and see ref. 12). However, in all three Kan^r derivatives of 128C53 examined after transfer of pVW3JI into this strain, no band corresponding to pVW3JI was visible (Fig. 1 track *c*): furthermore, the smaller of the two plasmids (MW 19×10^7) visible in strain 128C53 (Fig. 1 track *b*) had also disappeared. An identical plasmid pattern was observed in Kan^r derivatives of 128C53 obtained after the transfer of pVW5JI (MW 16×10^7) into this strain. However, when the P1-group plasmid pJB3JI was transferred into strain 128C53 (Fig. 1, track *e*) the two resident plasmids of strain 128C53 remained visible and in addition there was a band corresponding in mobility to that of pJB3JI.

The simplest interpretation that is consistent with both the genetical and physical observations described is that the smaller plasmid of strain 128C53 is the likely carrier of the linked Nod⁺ and Hup⁺ determinants. We term this plasmid pRL6JI, and we propose that pRL6JI recombined (or co-integrated) with the introduced plasmid to form a transmissible plasmid carrying determinants for Nod⁺ and Hup⁺ from pRL6JI, Kan^r from

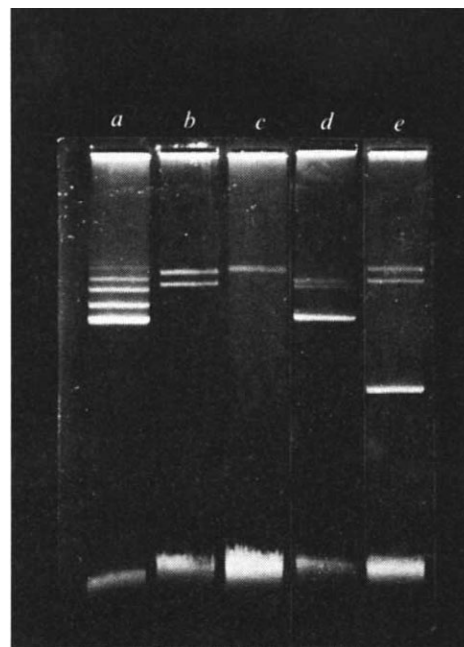


Fig. 1 Physical interaction between pVW3JI and a plasmid from strain 128C53. See Tables 1 and 2 for a description of the relevant strains. Lysates were prepared and analysed by electrophoresis on agarose gels following the method of Hirsch *et al.*¹². In each track the fastest migrating band represents sheared (chromosomal) DNA. *a*, Strain 2515. The plasmid band corresponding to pVW3JI is the second-fastest migrating plasmid band. The two high molecular weight plasmids of strain 300 are just visible on this gel (see ref. 12). *b*, Strain 3854 = 128C53 *rif-397*. *c*, Strain 3856 = 3854 carrying *kan* determinant from pVW3JI. *d*, Strain 3892 = kan^r Nod⁺ Fix⁺ Hup⁺ transconjugant from the cross 3856 × 16015. *e*, Strain 3955 = 3854 pJB3JI. Two tracks have been removed from this gel corresponding to lysates from 3957 (pVW5JI derivative, identical to track *c*) and 16015 (identical to track *d*).

pVW3JI (or pVW5JI) and Fix⁺ determinants from either or both moieties. The failure to detect the recombinant plasmid as a band on agarose gels might be due to the fact that its very large size (MW > 30 × 10⁶) would make it too susceptible to breakage to be recovered intact in our plasmid preparations. Inter-plasmid recombination might have occurred if pRL6JI shared homologous sequences with pVW3JI and pVW5JI.

There are at least two explanations for the fact that the introduced plasmid was never observed in Kan^r derivatives of strain 128C53. Either the introduced plasmids are incompatible with pRL6JI which itself might carry genes essential for the growth of this strain or, alternatively, pVW3JI or pVW5JI might be incapable of autonomous replication within this host. Both possibilities are consistent with the relatively low initial transfer frequency (10⁻⁴) of the transmissible plasmids into strain 128C53 and with the observed disappearance of the band corresponding to pRL6JI from Kan^r transconjugants.

Table 2. Quantitative measurements of pea root nodule activity following inoculation with Hup⁺ and Hup⁻ strains of *R. leguminosarum*

Inoculant	Acetylene reduction (μ mole C ₂ H ₄ per plant per h)	Hydrogen evolution (μ mole H ₂ per plant per h)	Tritium incorporation (μ mole H-T per g-nodule fresh wt per h)
300	5.11 (± 0.32)	3.16 (± 0.23)	0.002 (± 0.001)
300 pRL3JI	8.81 (± 0.77)	4.57 (± 0.69)	0.001 (± 0.001)
3740	8.46 (± 0.24)	5.01 (± 0.30)	0.001 (± 0.001)
128C53	7.97 (± 0.99)	0.57 (± 0.20)	0.738 (± 0.063)
3892	6.84 (± 0.48)	0.32 (± 0.04)	1.013 (± 0.112)
3894	9.43 (± 1.09)	0.37 (± 0.04)	0.844 (± 0.074)

'Alaska' peas grown in modified Leonard-jar assemblies were assayed 25 days after inoculation as previously described⁸. Tritium incorporation by nodulated roots was measured in 25-ml incubation vessels containing tritiated hydrogen gas (2.4%, v/v, 2.4 mCi mmol⁻¹) in the presence of acetylene (10%, v/v) to inhibit hydrogen production by nitrogenase⁹. Incubation was for 30 min and means ($\pm$ s.e.) were computed for six replicates. Bacteria recovered from surface-sterilized nodules were tested for the appropriate drug-resistance markers and plasmid patterns. Strains 3740, 3892 and 3894 were all Nod⁺ Kan^r derivatives of strain 16015. In strain 3740, which was Hup⁻, *kan* was derived from pVW5JI and *nod* from strain 300 (see ref. 13 for the construction of this strain). In strains 3892 and 3894, *kan* was derived from pVW3JI and pVW5JI respectively, *nod* and *hup* determinants were derived from 128C53 (see Table 1).

The plasmids of the 300 Nod⁻ strain 16015 have already been described^{12,14}. In the Kan^r derivatives that were Nod⁺ Hup⁺, no new plasmid bands could be seen (Fig. 1 track d). This implies either that any co-transferred plasmid co-migrated on gels with a resident plasmid from strain 16015 or that the co-transferred plasmid was too large to be visualized on gels (as was suggested for the donor strain itself). However, Kan^r 16015 derivatives that were Nod⁻ (Table 1b) contained a new plasmid band present in neither strain 16015 nor in the donor strain, but corresponding in size to the original plasmid band of pVW3JI as seen in lysates of normal strain 300 derivatives (Fig. 1 track a). In these cases it seems that the original pVW3JI plasmid may have been regenerated by a reversal of the original recombination event that caused its disappearance from derivatives of 128C53.

We have demonstrated that two apparently unrelated symbiotic phenotypes, nodulation ability for peas and the presence of hydrogenase activity, are genetically linked in strain 128C53. It is possible that a large proportion of the genes concerned specifically with the nitrogen-fixing symbiosis, the so-called symbiotic genes, will be found to be clustered and located on one or a few plasmids. Such an arrangement would certainly make it easier to develop genetically improved strains of *Rhizobium*.

This work was supported in part by NATO grant 1533 and by US NSF grant PFR77-07301. We thank Dr M. G. Yates and Professor J. R. Postgate for help and advice on the measurement of tritium incorporation by root nodules, Miss E. A. Wood for technical assistance, and Professor D. A. Hopwood for criticism of the manuscript.

Note added in proof: A. H. Christensen and K. R. Schubert (personal communication) have informed us that their culture of 128C53 (obtained from Dr J. C. Burton) has a different plasmid profile from that described here for our culture of this strain. It is not clear whether our Hup⁺ strain has undergone plasmid rearrangements during its history or whether two different strains exist bearing the designation 128C53.

Received 25 July; accepted 17 September 1980.

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Nonrandom segregation of nucleolar organizing chromosomes at mitosis?

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The random assortment of non-homologous chromosomes at meiosis is one of the fundamental tenets of genetics, to which few exceptions have been documented¹. The segregation of mitotic chromatids is believed to be similarly random. We report here that we seem to have discovered a new exception to this rule, in that nucleolar organizing chromosomes remain associated with one another, held in the same lateral orientation, for several mitotic cycles.

Five pairs of human chromosomes (nos 13, 14, 15, 21 and 22) carry rDNA sequences in specific chromosome segments, known as nucleolar organizing regions (NORs). The chromosomes are all acrocentrics, and the NORs are on their short arms. More than one chromosome may participate in the formation of a single nucleolus, DNA from their NORs uncoiling and extending deep into the substance of the nucleolus². During mitosis, the nucleoli disappear, but the chromosomes may be seen at metaphase grouped together with their short arms in close proximity. These configurations are called 'satellite associations' (ref. 3). A very close association of nucleoprotein complexes between associated chromosomes has been demonstrated autoradiographically⁴.

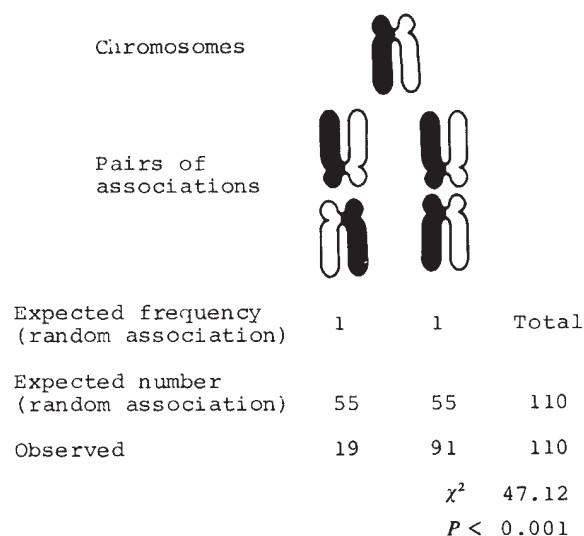


Fig. 1 Expected and observed satellite-association pairs in second-generation BUdR-substituted cells.

Methods have recently been developed which differentially stain the two chromatids of each chromosome. Cells grown in the presence of bromodeoxyuridine (BUdR) incorporate this base into their DNA in place of thymidine, and such BUdR-substituted chromatids stain less intensely with the dye 33258-Hoechst⁵, or with a combination of 33258 and Giemsa⁶. By growing cells in BUdR-containing medium for two cell cycles, chromosomes are produced with one chromatid half-substituted and one fully substituted with BUdR. The 'old' and 'new' chromatids can be differentially stained. After a third round of

DNA replication in the presence of BUdR, one-quarter of the chromatids will still be thymidine containing and darkly stained; half of the chromosomes will therefore have differentially stained chromatids, and the other half will consist of two bifilarly substituted, poorly stained chromatids.

We have examined satellite-associated chromosomes in both second- and third-generation BUdR cells, using standard peripheral blood chromosome cultures from five normal people. (Similar observations were made on a culture from an orangutan, although these cells are not included in the totals scored.) To minimize subjective scoring bias, we selected satellite associations consisting of only two chromosomes, where the chromosomes were closely paired (less than about 1 chromatid width apart), directly end-on to one another, and reasonably straight. All such configurations were scored. In second-generation cells, either a dark-to-dark or dark-to-light chromatid alignment may be seen, and assuming random segregation of chromatids at mitosis, these should be equally common. Our observations on 110 associations are set out in Fig. 1. It is clear that there is a highly significant tendency for old, thymidine-containing, darkly staining chromatids to be aligned with one another. There is about a 17% frequency of discordant (dark-to-light) associations. This may be an underestimate of stability, as many of the 17% exceptional associations seemed to be minimally twisted, but these were, nevertheless, scored as 'discordant' to avoid any possibility of artificially inflating the rate of concordant segregation.

In the absence of sister chromatid exchanges near the centromere, metacentric chromosomes generally show the dark-staining strand to go straight, rather than diagonally, across the centromere. In a purely descriptive sense, pairs of associated acrocentric chromosomes are behaving like single metacentric chromosomes with a centromere breakage rate of ~17% per cell cycle.

It is similarly simple to define the expected frequencies of various configurations in third-division cells, on the assumption either of random assortment or of a given dissociation rate per

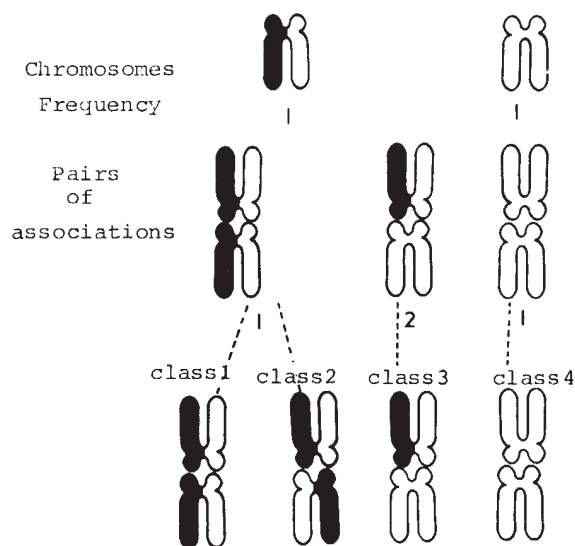


Fig. 2 Expected and observed satellite-association pairs in third-generation BUdR-substituted cells. If association pairs dissociate at the rate 'p' per cell cycle, and single chromosomes reassociate at random, the frequencies of the four classes of association after three cell cycles can be calculated as:

$$\text{Class 1} = \frac{1}{8}(4 - 7p + 6p^2 - 2p^3)$$

$$\text{Class 2} = \frac{p}{8}$$

$$\text{Class 3} = \frac{1}{2}(3p - 3p^2 + p^3)$$

$$\text{Class 4} = \frac{1}{4}(2 - 3p + 3p^2 - p^3)$$

The 'expected' values in the last line of the figure are derived by substituting $p = 0.2$ in these formulae. NS, not significant.

Expected frequency (random association)	$\frac{1}{2}$	$\frac{1}{2}$	2	1	Total
Expected number (random association)	6.25	6.25	25	12.5	50
					χ^2 18.04
					$P < 0.001$
Expected number (20% dissociation)	17.6	1.3	12.2	18.9	50
					χ^2 7.08
					NS
Observed	15	4	15	16	50

cell cycle with random rejoining of dissociated chromosomes. These expectations, and our observations on 50 relevant associations, are set out in Fig. 2. The data clearly fit well with the observations on second-division cells.

The staining of a chromatid in this system depends on the presence of either thymidine or BUdR in a single DNA strand. Similar staining of opposed chromatids therefore implies that they are being held in alignment during mitosis by forces operating at the level of the single DNA strand.

There are several possible explanations for this phenomenon. (1) Chromatids of associated chromosomes may be held oriented relative to one another by the establishment of physical connectives within the nucleolar substance. The existence of ribonucleoprotein connections has been demonstrated⁴. Inter-chromosomal DNA connections have also been reported, and have led to suggestions of the same DNA strand continuing through more than one chromosome⁷, although there is now a strong suspicion that these interchromosomal fibres are artefacts⁸. Our observations require that single DNA strands are held together for several cell cycles, and it is easier to envisage such a rigid orientation from a nucleic acid connection than from mere enmeshment in a common nucleoprotein matrix. (2) One cannot exclude the possibility that chromatids do segregate randomly at mitosis, but that their involvement in new satellite associations is nonrandom, thymidine-containing chromatids selectively aligning opposite one another. Even this implies a pairing phenomenon at the level of the single DNA strand. The restrictions on joining imposed by DNA strand polarity would not adequately explain our observations, as the number of active nucleolus-organizing chromosomes per cell is such that there would almost always be both thymidine- and BUdR-containing strands of each polarity available. (3) Presumably, not all nucleolus-associated chromosome groups survive into metaphase as visible satellite associations, but there seems to be no reason that 'concordant' pairs should be more likely to survive than 'discordant' pairs.

Any attempt to choose between these possibilities, or to consider the basic mechanism of this phenomenon, would be purely speculative. However, the most economic hypothesis seems to be that a physical continuity, at the DNA single-strand level, is actually established between non-homologous chromosomes, and can persist through several cell cycles.

The most common form of chromosome rearrangement in man is the Robertsonian fusion, in which acrocentric chromosomes become permanently joined by their short arms, the translocation chromosomes sometimes remaining demonstrably dicentric. Such translocations may segregate to produce aneuploid offspring, particularly Down's syndrome. If the NOR-bearing chromosomes regularly establish physical connections with one another, this may be related to the generation of such translocations.

There are conflicting data on the randomness with which particular chromosomes are involved in satellite associations⁹, and on whether such associations are causally related to the production of trisomic children¹⁰⁻¹². If such a relationship does exist, it may also be concerned with the phenomenon of intimate chromosome association described here.

We thank H. J. Evans for useful comments. This work was supported by a programme grant from the MRC.

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Human T lymphocytes of inducer and suppressor type occupy different microenvironments

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Distinct subsets of human peripheral T-cell populations have recently been characterized using mouse monoclonal antibodies and conventional hetero-antisera in functional tests *in vitro*¹⁻⁶. 'Inducer' or 'helper' T cells have been shown to react with a monoclonal antibody termed OKT4. These OKT4⁺ cells respond to soluble antigens³, help B-lymphocyte differentiation into plasma cells in pokeweed mitogen stimulated cultures⁴ and assist the development of cytotoxic T cells in mixed lymphocyte cultures (MLC)⁵. In contrast, the 'suppressor-cytotoxic' T-cell subset is recognized by the monoclonal antibodies OKT5⁵ and OKT8⁶. The same subset can also be labelled with a conventional horse antiserum which (after extensive absorption) recognizes TH₂ antigen^{5,7}. These OKT8⁺, TH₂⁺ cells fail to respond optimally to soluble antigen³ but contain the concanavalin-A induced suppressor cell population^{5,7} and the cells which develop cytotoxic activity in mixed lymphocyte reaction (MLR)-induced cell-mediated lympholysis³. The physiological role, tissue distribution and recirculation patterns of 'inducer' and 'suppressor' T cells are unknown, although changes in the proportion and activity of blood-borne T-cell subsets have been observed in various immunoregulatory disorders^{8,9}. We have therefore now analysed the distribution of these T-cell subsets in the lymphohaematopoietic organs and the gut. OKT4⁺, OKT8⁻ cells of inducer type predominate in the thymic medulla, blood and T-cell traffic areas such as tonsillar paracortex and intestinal lamina propria. OKT4⁺, OKT8⁺ cells of suppressor-cytotoxic type, on the other hand, constitute the larger part of T-cell population in normal human bone marrow and gut epithelium. Furthermore, a close micro-anatomical relation can be seen between the OKT4⁺, OKT8⁻ T cells and non-lymphoid cells expressing large amounts of Ia-like (p 28, 33) antigens, for example, interdigitating (ID) cells and Ia⁺ macrophages, suggesting that Ia-like antigens may play a part in the local regulation of inducer T cell activity. Thus the T-cell subsets which have been shown to have different functions *in vitro* seem also to have different patterns of tissue distribution, implying different immunological functions *in vivo*.

The principle of the study was to apply well characterized antibodies from different species in various combinations using second layer antibodies coupled with different fluorochromes (fluorescein-isothiocyanate FITC: green and tetramethylrhodamine isothiocyanate TRITC: red) in order to determine whether the antibodies detect identical, overlapping or distinct populations. Table 1 shows the distribution of OKT4⁺ and OKT8⁺, TH₂⁺ T lymphoid cells analysed in cell suspensions. Preliminary experiments showed that all three reagents (OKT4, OKT8 and anti-TH₂) reacted exclusively with T-lymphoid cells which were identified with a rabbit antiserum reacting to human T-lymphocyte antigen (HuTLA⁺; Table 1). These findings confirmed that the antibodies were T-lineage markers^{1-6,10}. Furthermore, the OKT8 and anti-TH₂ antibodies labelled the same populations (>98% double-labelled cells). Thus these two reagents were used interchangeably in this study.

In the human thymus 78% of all cells were OKT4⁺, TH₂⁺ (see also refs 1–6). The majority (80%) of these double-labelled cells expressed nuclear terminal deoxynucleotidyl transferase (TdT), a marker of cortical thymocytes¹¹. 20% of the OKT4⁺, TH₂⁺ population was TdT⁺.

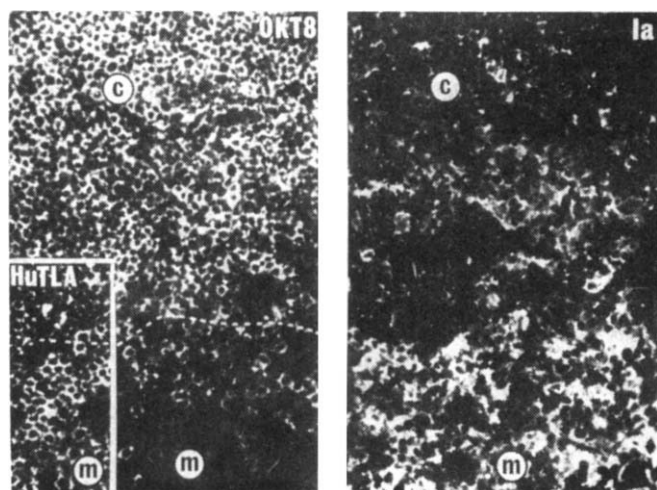


Fig. 1 Cells in the human thymic cortex (c) and medulla (m) reacting with antisera to OKT8 (OKT8, a mouse monoclonal antibody), to human thymocyte/T-cell antigen (HuTLA; a rabbit antiserum) and to Ia-like p 28, 33 antigen (Ia; a chicken antiserum detecting core determinants of p 28, 33)^{11,12}. Sections of frozen tissue biopsies from infant thymus were fixed for 10 min in ethanol and washed in saline¹¹. OKT8 (1:100 dilution) and chicken anti-Ia-like antiserum (1:40) were added, incubated for 30 min at room temperature and washed for 30 min. Goat anti-mouse Ig-FITC (affinity purified antibody; 0.5 mg ml⁻¹) and sheep anti-chicken Ig-TRITC (1:20 dilution) were added for 30 min and washed again. The same areas were photographed with filters for FITC (OKT8) and TRITC (Ia). The broken line indicates the cortico-medullary boundary. Insert shows the same area photographed in an adjacent section. This had been incubated with anti-HuTLA (1:20 dilution), washed and stained with goat anti-rabbit Ig-FITC (1:40 dilution). OKT8 reacts with virtually all cortical thymocytes and 20% of medullary thymocytes. Anti-HuTLA detects all thymocytes. Anti-Ia stains cortical epithelial cells strongly and large medullary cells corresponding to interdigitating cells (ID) very strongly. $\times 200$.

Within the population of thymic cells with only a single label (putative thymic medullary lymphocytes; see below), the OKT4⁺, TH₂⁺ cells were more frequent (76%) than the OKT4⁺, TH₂⁺ cells (24%). Previous studies^{1–6} suggested that the majority of T cells in peripheral human blood are either OKT4⁺, TH₂⁺ or OKT4⁺, TH₂⁺, although the existence of a few double-labelled cells has not been formally excluded. Our study has extended these previous findings (Table 1). The calculated proportions of OKT4⁺, TH₂⁺ cells (inducer phenotype) within the HuTLA⁺ T-lymphoid population were 66% in blood, 64% in tonsil and 13% in bone marrow from children. In contrast, the proportions of OKT4⁺, TH₂⁺ cells (suppressor-cytotoxic phenotype) were 27% in blood, 20% in tonsil and 82% in bone marrow. A small number of double-labelled OKT4⁺, TH₂⁺ lymphocytes were found in the periphery—2.6% of blood T cells and 6.5% of tonsil T cells. (These cells could have been immature T cells but they failed to express cortical thymocyte markers such as TdT and reactivity with monoclonal antibody to cortical thymocyte antigen, HTA-1^{11,12}.) Thus the definition of 'inducer' and 'suppressor-cytotoxic' T subsets with the available reagents in man seems to be more convenient and distinct than the definition of corresponding cell types in the mouse where large proportions (20–50%) of peripheral T cells simultaneously express 'inducer' (Ly-1) and 'suppressor' (Ly-2,3) markers^{14,15}.

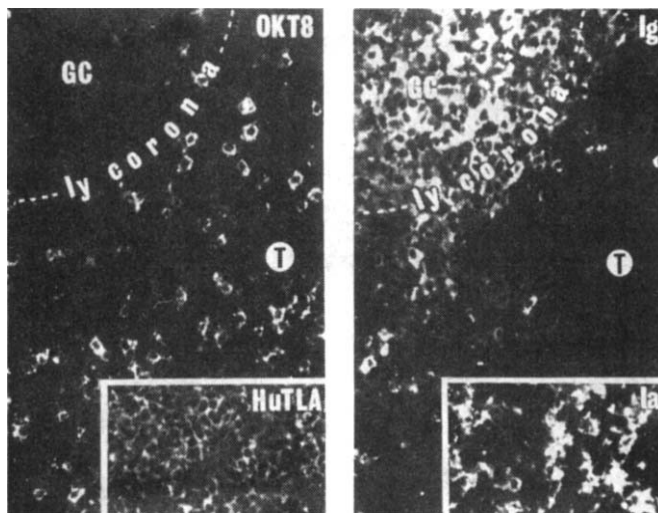


Fig. 2 Cells in the human tonsil reacting with antisera to OKT8 (OKT8), to immunoglobulin (Ig), to human T-cell/thymocyte antigen (HuTLA) and to Ia-like p 28, 33 antigen (Ia), GC, germinal centre, containing lacy deposits of immunoglobulin; ly corona, lymphocyte corona containing Ig⁺ B lymphocytes; T, paracortical area with T cells which are HuTLA⁺ (see insert); only 20% of these T cells react with OKT8. In this area large ID cells stain brightly for Ia (see insert). The reagent combinations were OKT8 (FITC) together with goat anti-human IgM (TRITC; a purified antibody used at 0.5 μ g ml⁻¹), and HuTLA (FITC) with Ia (TRITC). The same areas were photographed with selective filters. $\times 200$.

An immunohistological analysis of T-cell subsets was performed using OKT8 antibody with an affinity purified goat anti-mouse Ig-FITC. Bright membrane staining was obtained on a subset of lymphoid cells in sections of frozen biopsies. The OKT8 antibody could also be used in double-marker combinations with rabbit anti-HuTLA antiserum and other reagents (Figs 1–3). Since the OKT4 antibody showed only weak staining in tissue sections of peripheral lymphoid organs, T-cell subsets of 'inducer' and 'suppressor-cytotoxic' type were defined as HuTLA⁺, OKT8⁺ and HuTLA⁺, OKT8⁺, respectively.

In the thymic medulla, 60–75% of HuTLA⁺ cells were OKT8⁺ (Fig. 1). This is consistent with the cell suspension analysis discussed earlier (Table 1), indicating that the majority of mature thymic medullary lymphocytes express the 'inducer' phenotype. Note that some of the medullary OKT8⁺ cells may be recent arrivals from the cortex which express TdT and cortical thymocyte antigen HTA-1¹¹. These cells, which represent 6–15% of the medullary cell population, may not have

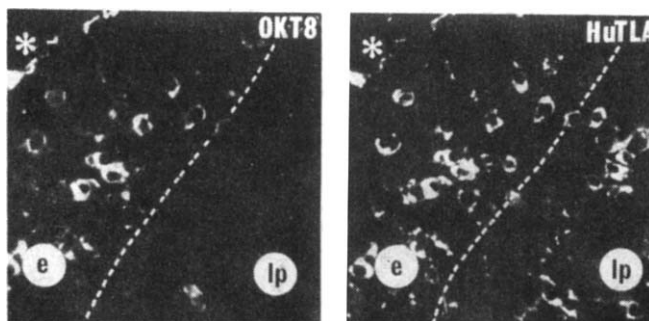


Fig. 3 Cells in the human jejunum reacting with antisera to OKT8 (OKT8) and to human T-cell/thymocyte antigen (HuTLA). e, Epithelium; lp, lamina propria. (*) intestinal lumen. Most intra-epithelial lymphocytes are double-stained for HuTLA and OKT8 ('suppressor-cytotoxic' phenotype). In the lamina propria many T cells are HuTLA⁺, OKT8⁺ ('inducer' phenotype). $\times 220$.

Table 1 Distribution of T lymphoid cells expressing the inducer (OKT4⁺, TH₂⁺, OKT8⁻) and 'suppressor-cytotoxic' (OKT4⁻, TH₂⁻, OKT8⁺) phenotypes

	No. of cases	% Labelled with rabbit anti-HuTLA*	% Of cells labelled with mouse OKT4 and horse anti-TH ₂ (SUP) antibodies				% Labelled with mouse OKT8†
			All cells labelled‡	OKT4 ⁺ only	TH ₂ ⁺ only	OKT4 ⁺ , TH ₂ ⁺ double	
Thymus	5	96 ± 2.1	89 ± 0.8	8.5 ± 0.9	2.7 ± 0.5	78 ± 3.7	80
Peripheral blood¶	7	75 ± 3.3	72 ± 3.1	50 ± 1.9	20 ± 1.5	2.0 ± 0.4	23
Tonsil*	4	60 ± 5.6	55 ± 5.1	39 ± 1.8	12 ± 2.3	3.9 ± 1.3	17
Bone marrow**	6	4.5 ± 0.9	4.4 ± 0.2	0.6	3.7 ± 0.2	0.1	5

10⁶ cells in 50 µl buffered saline were incubated with conventional antisera (1:20 dilution) and monoclonal antibodies (peritoneal exudate; 1:200 to 1:500 dilution), washed twice and reincubated with goat anti-mouse-Ig-TRITC and goat anti-rabbit or horse Ig-FITC (1:20 dilution), followed by washing and counting the labelled cells under a fluorescence microscope.

* A rabbit antiserum reacting with human thymocytes/T cells was made against monkey thymocytes and extensively absorbed (with human red cells, liver powder, chronic lymphoid leukaemia and lymphoid cell lines of B type and acute myeloid leukaemia; ref. 12). The second layer used (goat anti-rabbit-Ig) was conjugated to FITC. The horse anti-HuTLA prepared from an anti-human thymocyte globulin (ATGAM; Upjohn, Lot 17.923) with similar absorptions gave identical results. Values are mean ± s.e.m.

† These percentages are consistently lower than the proportion of HuTLA⁺ cells in the same sample. The HuTLA⁺, OKT4⁻, TH₂⁻ cells appear to be larger blasts in the thymus (prothymocytes? see refs 6, 11, 13) and small lymphocytes of unknown function in the blood and tonsils.

‡ Horse anti-TH₂ serum was prepared from horse anti-HuTLA serum at the Royal Free Hospital by further absorption with OKT4⁺ leukaemic lymphocytes obtained from a patient with chronic lymphocytic leukaemia of T-cell type. This reagent gave identical results to the control horse anti-TH₂ reagent (see ref. 7).

§ Similar double-labelling experiments using anti-TH₂ and OKT8 showed that these two reagents reacted with an identical population of cells; >98% of labelled cells in thymus, blood and tonsil were reactive with both antisera.

|| Infant thymus cell suspensions from patients undergoing elective cardiac surgery.

¶ Normal donors of 30–42 years of age.

* The donors (10–15 yr) had tonsillitis in the past. The tonsillectomy was performed after antibiotic treatment.

** From children (5–15 yr). No haematological abnormality.

yet matured into OKT8⁻ lymphocytes. There was an abundance in the medulla of non-lymphoid cells which strongly expressed Ia-like (p 28, 33) antigens. Some of these could be Ia⁺ epithelial cells which were also present in the cortex. Nevertheless the most brightly stained population appeared to be a group of interdigitating (ID) cells with prominent veils and processes^{11,16}. These Ia⁺ cells could also be detected in the interlobular septae and may have been migrating cells (Fig. 4 and refs 11, 17).

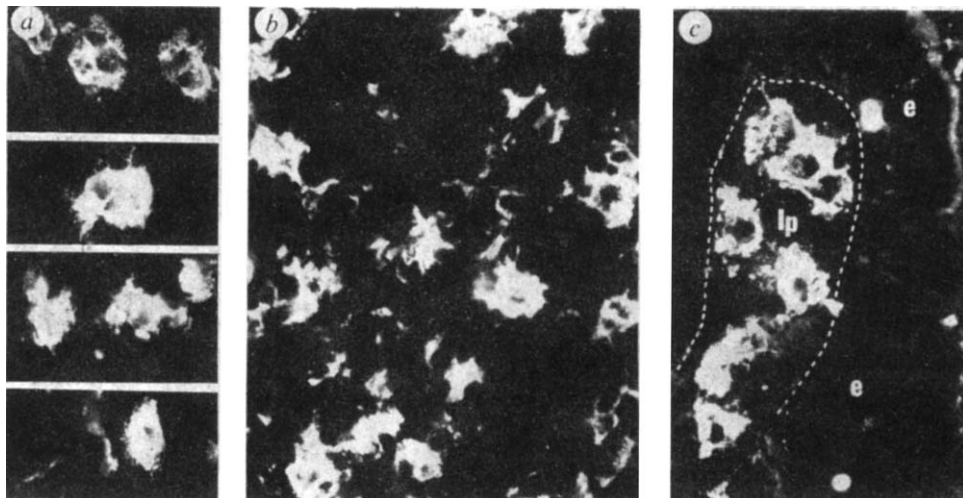
In serial sections of tonsil the germinal centres (which contained lacy deposits of immunoglobulin complexes surrounded by a B-lymphocyte corona) and paracortical T-cell areas were identified (Fig. 2). In the B-lymphocyte corona less than 5% of cells were HuTLA⁺. This small T-lymphocyte population contained both OKT8⁺ and OKT8⁻ cells. In the paracortical areas 70–80% of HuTLA⁺ cells were OKT8⁻ and 20–30% were OKT8⁺. In these areas large ID cells expressed Ia-like antigens very strongly (Figs 2 and 4; see also refs 18–20). It appeared that the Ia⁺ ID cells were preferentially surrounded by OKT8⁻ T lymphocytes and tended to be apart from the OKT8⁺ cells. Further studies will be needed to determine

whether isolated ID cells form rosettes with T lymphocytes of the 'inducer' or 'suppressor' phenotype.

Finally, histologically normal jejunal biopsies were studied from patients undergoing investigation of diarrhoea. In the lamina propria the HuTLA⁺ population contained more OKT8⁻ cells than OKT8⁺ cells (65–75% OKT8⁻ T cells in the three samples studied; Fig. 3). When adjacent sections were stained for Ia-like antigens, the abundant macrophages in the lamina propria stained very strongly for Ia-like antigens (Fig. 4) and resembled the light microscopic appearance of Ia⁺ ID cells observed in tonsils or in the thymic medulla and septae. Furthermore, the intra-epithelial lymphocytes in human gut have recently been shown to be almost exclusively HuTLA⁺ T lymphocytes²¹. In contrast to the T cells in the lamina propria, this intra-epithelial T-cell population consisted mainly of OKT8⁺ cells (70–90% OKT8⁺ cells within the HuTLA⁺ population in the three samples analysed).

The observations outlined above are compatible with the view that subsets of peripheral T lymphocytes develop from immature OKT4⁺, OKT8⁺ thymocytes through a series of

Fig. 4 Interdigitating (ID) cells and macrophages in the human thymus (a), tonsil (b) and gut (c). All three preparations are sections from frozen biopsies stained for human Ia-like (p28, 33) antigen with chicken-anti-Ia-like serum (1:40) followed by sheep anti-chicken Ig-TRITC (1:20). a, Areas of interlobular septae contain ID cells (migrating cells?) which resemble circulating lymph-borne veiled cells²⁸. The cells exhibit characteristic strongly Ia⁺ 'veils' and 'whiskers'. Similar cells are seen around the cortico-medullary junction within the thymus (see Fig. 1). b, A paracortical area from tonsil. The Ia⁺ ID cells again show extensive processes which surround the T lymphocytes (not stained, but see insert in Fig. 2). c, A jejunal villus with epithelium (e) very weakly stained for Ia-like antigen and lamina propria (lp) containing large macrophages with abundant Ia-like antigens. The staining patterns suggest that the expression of Ia-like antigens might be cytoplasmic in many of these cells. ×315.



differentiation steps^{6,13}. The preponderance of OKT8⁺ T cells in the bone marrow suggests that T cells are normal inhabitants of this tissue with a definite physiological role (suppression of immunoglobulin synthesis?) rather than representing contaminating blood-borne T cells.

Intriguingly, while the OKT8⁺ subset shows 'affinity' to the gut epithelium which expresses Ia-like antigens poorly, the lymphoid microenvironments (thymic medulla, paracortex, lamina propria) which contain high proportions of 'inducer' T cells exhibit large numbers of Ia⁺ non-lymphoid cells. These stain more brightly for Ia-like antigens than B lymphocytes, dendritic cells in the germinal centres or sinus histiocytes²⁰. In the literature these cells are variably referred to as ID cells^{15-19,22,23}, cells of the cortico-medullary junction²⁴ or macrophages of the lamina propria^{21,25}. Further immuno-electron microscope studies are needed to determine the ultrastructural characteristics, lineage derivation (from marrow precursors? see ref. 26) and cytoplasmic Ia-content (secretion or shedding of Ia?) of this apparently migratory Ia⁺ population. It is already known that at least a proportion of ID cells contain Birbeck granules and are related to skin Langerhans cells^{23,27} and circulating 'veiled' cells in the lymph^{27,28}. These cells all express large amounts of Ia-like antigens²⁸⁻³⁰. The full characterization of this strongly Ia⁺ ancillary system for 'inducer' T lymphocytes throughout the body is important since Langerhans cells have already been shown to play a part in transporting foreign antigens from skin to the regional lymph nodes and to 'present' these antigens to T cells^{28,29,31}. A similar role could be postulated for the lamina propria macrophages, the 'Cinderella' cells of the gastrointestinal system²⁵.

It is also known that 'inducer' T cells see foreign antigens in the context of Ia antigen (in the mouse)³² or Ia-like HLA-DR antigens (in man)³³ according to the previous thymic education of these cells³². In both species, thymic cortical epithelial cells as well as medullary ID cells express large quantities of Ia or Ia-like antigens^{11,34}. The close anatomical relation of 'inducer' T cells and Ia⁺ cells in the tonsil and gut further suggests that this physiological control of T-cell recognition is maintained in the peripheral lymphoid tissues.

The use of well characterized monoclonal antibodies to T-cell subsets in studies of both cell suspensions and tissue sections of biopsies taken from patients with viral infections, immunoregulatory ('autoimmune') disorders and graft-versus-host disease may well contribute to the understanding of virus control and disease development^{7,8,35}.

We thank Dr F. J. Bollum for anti-TdT antibody and Professor S. F. Schlossman for a sample of anti-TH₂ antiserum. Human thymus and bone marrow samples were provided by Mrs L. Layward and Dr N. Rapson of the Institute of Child Health and Dr H. G. Prentice of the Royal Free Hospital, London. Gut biopsies were obtained in collaboration with Dr D. Jewell, Royal Free Hospital, London. W.S.S. was supported by the Coppleston Postgraduate Medical Foundation.

Received 20 June; accepted 16 September 1980.

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Different postsynaptic events in two types of retinal bipolar cell

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The first synapse in the vertebrate visual system is made between the photoreceptors and the bipolar cells. Bipolar cells fall into two distinct classes according to whether the cell hyperpolarizes or depolarizes to small centred spots of light. Most evidence indicates that the light-induced hyperpolarization of the photoreceptors suppresses transmitter release from the synaptic terminals¹⁻³, and it is probable that the differences between the two bipolar cell classes results from the different actions of the photoreceptor transmitter⁴. In analysing the membrane potential fluctuations in both types of bipolar cell we find that the voltage noise spectra differ. It is to be expected that postsynaptic noise would be composed of the sum of noise generated in and transmitted from the cones^{5,6} and the noise arising from the statistical nature of synaptic transmission. We report here evidence for two such components in the voltage noise spectra recorded from each type of bipolar cell. The differences in the frequency distribution of the presumed transmitter-related components indicates that the transmitter generates events of longer duration in the depolarizing bipolar cells.

Eye cup preparations from the snapping turtle (*Chelydra serpentina*) were mounted in a chamber through which moist oxygen flowed and such that small spots of light could be focused on the impaled cell⁷. Bipolar cells were recorded at depths of 120-180 μ m distal to the vitreal surface of the retina. A sample of studied cells were stained with either Procion yellow or Lucifer⁸ and all positively identified as bipolar cells. Although a rod input may be demonstrated in certain cells, we have investigated the red cone input only⁹. The stimulus was a 100 μ m spot of 650 nm light centred on the impaled cell.

In hyperpolarizing bipolar cells, steps of light reduced potential fluctuations¹⁰ (Fig. 1a). The total noise variance decreased 27-fold for this cell, from 1.1 mV² in the dark to 0.04 mV² in bright light. This reduction appears to reflect primarily the cutoff of the cone transmitter and cannot be attributed to a potential-dependent membrane resistance decrease since we find that the hyperpolarization is associated with an increase in cell input resistance. In addition, we find that hyperpolarization of the cell to the light evoked levels by extrinsic current does not suppress the noise in the dark.

The potential fluctuations were Fourier analysed to obtain a difference spectrum between the spectra in the dark and in the light. The difference spectra were found to have the same form at all light levels, the effects of illumination being to rescale their amplitude. A difference spectrum between dark and bright light

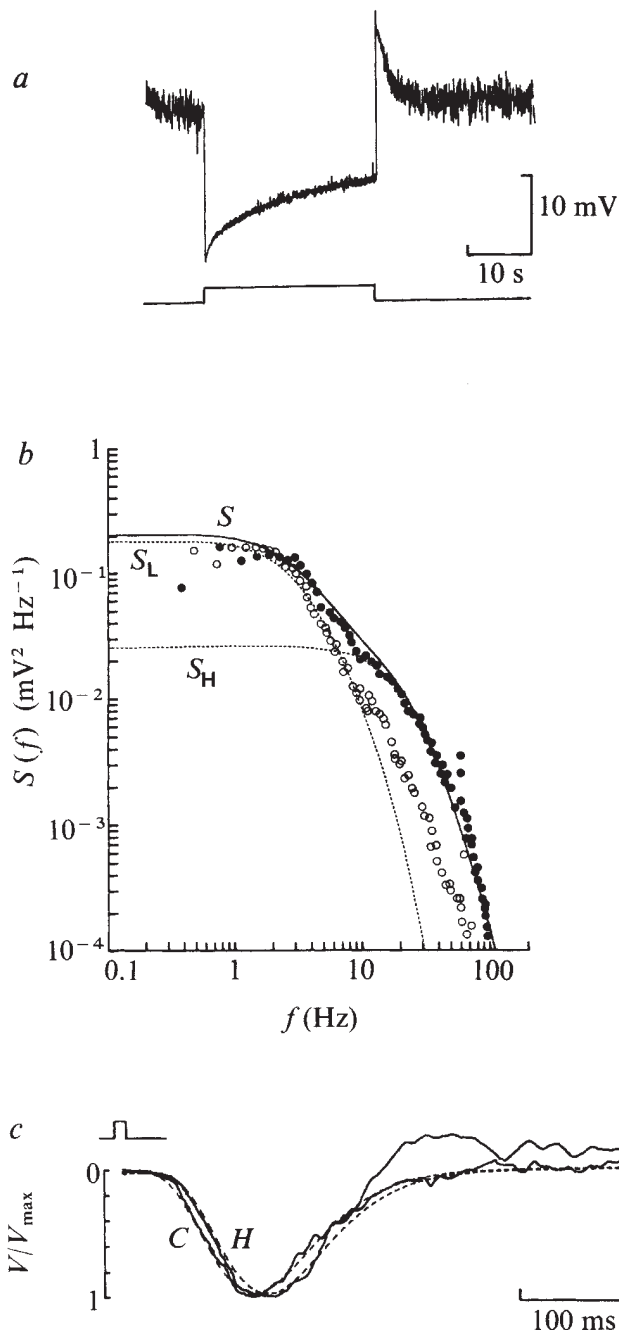


Fig. 1 Voltage noise in hyperpolarizing bipolar cells. *a*, Response of a cell to a 100- μm spot of 650-nm light with an intensity of 9.85×10^4 photons $\mu\text{m}^{-2} \text{s}^{-1}$. Maximum response to flashes; 21 mV. *b*, Difference spectrum (dark – bright) of the voltage noise for the hyperpolarizing bipolar cell (●) and a cone (○). The cone spectrum has been multiplied by a factor of 26 for normalization. The records were filtered at 100 Hz, and sampled at 400 Hz (bipolar cells) or 500 Hz (cones) for processing using a 1,024-point FFT program. The spectrum is frequency smoothed. The extracellular electrode noise variance was less than 0.01 mV^2 . The continuous curve S , is the sum of the two functions shown as dotted curves¹⁰: S_H is proportional to the modulus squared of the Fourier transform of equation (1) with $T = 5.9$ ms; S_L is the product of S_H and two lorentzian functions with time constants 54.9, 9.2 ms required to fit the cone spectrum⁶. The ratio of the variances associated with the components $S_L : S_H$ is, by numerical computation, 1.57 : 1. *c*, Signal-averaged and normalized responses of a cone and hyperpolarizing bipolar cell, both cells within their linear ranges. The dotted lines are C , seven-stage low-pass filter model with time constant per stage = 20 ms (ref. 5), and H , the function after passing through a filter given by equation (1) with $T = 5.9$ ms. The difference in times to peak is 13 ms.

is shown in Fig. 1*b* and falls off asymptotically as $1/f^4$ with more power at high frequencies than found in cones⁶. In some cells there was a very pronounced inflection at around 10 Hz and, unlike the voltage noise spectrum recorded in cones, the spectrum could not be fitted by the simple product of lorentzian functions⁶. Instead, the following model leads to a fit of the noise difference spectrum as a sum of two components, S_L and S_H . The release of transmitter from the cones and its postsynaptic action may be considered to be a shot process, and will result postsynaptically in a noise spectrum $S_H(f)$ (ref. 11). If the rate of transmitter release were a linear function of the presynaptic cone membrane potential, with fluctuations described by a spectrum $S_C(f)$ (ref. 6), it can be shown that there will be an additional term $S_L(f) = \text{constant} \times S_C(f) \times S_H(f)$ present in the spectrum of the postsynaptic fluctuations (compare ref. 11, equation 2.6–11). The term $S_L(f)$ will have power restricted to lower frequencies than $S_H(f)$ and arises because the synapse acts to filter the noise transmitted from the cones.

The simplest unitary event sufficient to describe the component S_H has the form $\alpha(t)$ given by

$$\alpha(t) = (\alpha/T) \exp(-t/T + 1) \quad (1)$$

where α is the amplitude, T the time to peak, is 5.9 ms and the event halfwidth is 14.5 ms. The spectrum associated with the event given by equation (1) is then

$$S_H(f) = \frac{S_H(0)}{(1 + 4\pi^2 T^2 f^2)^2} \quad (2)$$

$\alpha(t)$ is formally equivalent to the impulse response of a two-stage low pass filter¹², where both stages have the time constant T . One stage of this filter most probably represents the membrane time constant, τ . In a sample of nine cells we found $\tau = 9.2 \pm 5.0$ ms (mean $\pm$ s.d.). Hence, the likely duration of transmitter action corresponding to the second filter stage, would be no greater than 6 ms.

Equation (1) also describes the effective filter representing the cone–bipolar synapse. Figure 1*c* shows that the response in the hyperpolarizing bipolar cell can be predicted by simply passing the cone response through this filter. The early phase of the bipolar response is predicted well, corresponding to frequencies in the spectrum above 1 Hz. The overshoot in the repolarization of the bipolar cell response can be ascribed to an additional differentiation occurring for frequencies below about 1 Hz, which is not included in this model. Such a differentiating stage has also been postulated in the retinal signal pathway from the photoreceptors to account for some of the properties of ganglion cell firing patterns in the turtle retina¹³.

A similar analysis of the fluctuations may be made for depolarizing bipolar cells. Dim lights usually, but not always, produced an increase in intracellularly recorded voltage noise. In the cell shown in Fig. 2, the noise variance increased from 0.055 mV^2 to 0.154 mV^2 for a 1.5-mV depolarization, with an accompanying cell input resistance decrease¹. Further increase in the light intensity produced a noise suppression to a level close to that in the dark. The initial increase in noise might be expected if the postsynaptic action of transmitter were to block ionic channels¹⁴ and if a majority of the channels were blocked in the dark¹⁰.

Figure 2*b* illustrates the difference spectrum of voltage noise between dim light and the dark. Although, in contrast to the hyperpolarizing bipolar cells, there was no clearly indicated inflection point in the noise spectra, it was found that the noise had a narrower bandwidth than for hyperpolarizing bipolar cells or cones. A decomposition of the voltage noise spectrum was obtained by considering the synaptic filtering required to produce the delay in the flash response (Fig. 2*c*). The observed delay can be obtained using equation (1) with $T = 21$ ms as the synaptic filter, in which case the associated unitary voltage event would have a half duration of 49 ms. For the input time constant

of depolarizing bipolar cells, it was found that $\tau = 7.2 \pm 3.5$ ms ($n = 5$). The membrane time constant, $S_H(f)$, in the spectral decomposition (Fig. 2b) can be consistently interpreted as accounting for one stage of the filter if the duration of transmitter-activated conductance change is not less than 21 ms, corresponding to the other stage of the synaptic filter. Conversely, an upper bound for the duration of the event in the depolarizing bipolar cell can be obtained if the spectrum is fitted

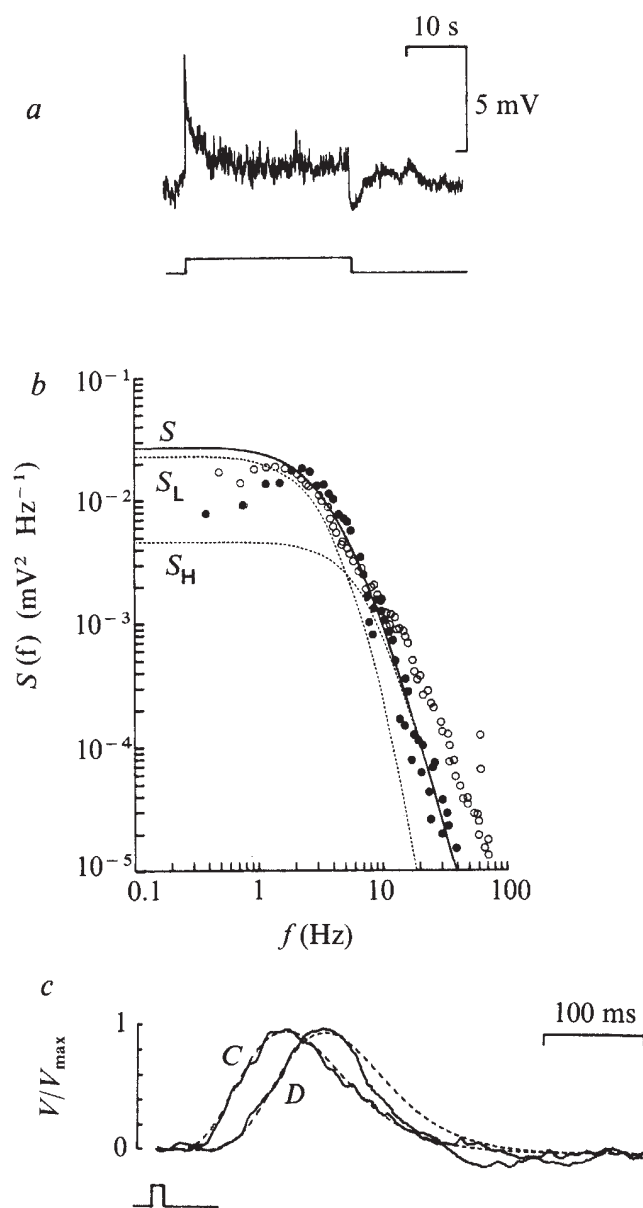


Fig. 2 Voltage noise in depolarizing bipolar cells. *a*, Response of a cell to a $100 \mu\text{m}$ spot with an intensity of $1,380 \text{ photons } \mu\text{m}^{-2} \text{ s}^{-1}$. Maximum response to flashes, 11 mV . *b*, Difference spectrum (dim - dark) of the voltage noise for the bipolar cell (●). Cone spectrum (○) as before, multiplied by 4.8 for normalization. The dotted curve S_H is obtained from equation (2) with $T = 21 \text{ ms}$. S_L is constructed as in the text. The ratio of the variances associated with the components $S_L : S_H$ is computed to be 2.66 : 1 to provide the best fit to the data. *c*, Normalized linear range responses to a flash of light in a cone (inverted) and the bipolar cell with computed cone *C* and bipolar cell *D* responses. The difference in time to peak between the responses is 41 ms . The hyperpolarization during recovery of the bipolar cell indicates differentiation at this stage of synaptic processing.

by a single component of the form of equation (2), which would lead to an event with a half duration of 82 ms . Thus it appears by either analysis that the transmitter event in the hyperpolarizing bipolar cell may be much shorter than in the depolarizing bipolar cell.

The differences in the temporal properties of the synapses between the two cell types may indicate that each is specialized for a different role. By recording ganglion cell spikes elicited by current injection into cones differences in the latency between the on- and off-pathways to the ganglion cells have been described¹³. It is possible that this functional difference may be established at the level of the outer plexiform layer. The wider passband of the cone-hyperpolarizing bipolar cell synapse may be appropriate for signals in the photopic range when the response of the photoreceptors themselves speed up¹².

However the narrower range of frequencies passed by the depolarizing bipolar cell synapse is matched closely to the temporal characteristics of the cell's response to a flash of light. Such an arrangement would be advantageous in the detection of light in the mesopic range.

We thank Drs Juan Korenbrot and Julie Schnapf for helpful comments on the manuscript. This work was supported by NIH grant EY-01869.

Received 7 April; accepted 20 August 1980.

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Somatostatin selectively inhibits noradrenaline release from hypothalamic neurones

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Somatostatin is a hypothalamic peptide hormone which inhibits growth hormone release from the anterior pituitary¹. However, biochemical and morphological investigations have revealed that somatostatin is located not only in the hypothalamus but also in other brain areas (for example the cerebral cortex) where it occurs and in nerve cell bodies and fibres²⁻⁵ from which it can be released in a Ca^{2+} -dependent manner⁶. It has therefore been suggested that the neuropeptide may have functions in the central nervous system other than its effect on growth hormone release⁷; one possible action is that of a neuromodulator^{4,6}. Therefore, hypothalamic and cerebral cortical slices of the rat were used to examine whether somatostatin modifies the electrically or CaCl_2 -evoked release of tritiated monoamines from monoaminergic neurones. It is reported here that somatostatin inhibits ^3H -noradrenaline release from the hypothalamus (but not from the cerebral cortex) but does not affect the release of ^3H -dopamine and ^3H -serotonin.

Slices of hypothalamus or occipital cortex (0.3 mm thick, diameters 2.0 and 3.0 mm , respectively) from male Wistar rats (200 – 300 g) were incubated for 60 min in physiological salt solution (of composition described in Fig. 1 legend) containing one of the following tritiated monoamines at a concentration of

0.1 μM : ^3H -(-)noradrenaline (21.3–25.4 Ci mmol^{-1}), ^3H -dopamine (32.6 Ci mmol^{-1}) or ^3H -serotonin (25 Ci mmol^{-1}). In these conditions the tritiated monoamines are selectively taken up into noradrenergic, dopaminergic and serotonergic neurones of the slices, respectively^{8–10}.

After incubation, the slices were superfused with either physiological salt solution or Ca^{2+} -free solution containing 25 mM K^+ (isomolar replacement of NaCl by KCl). Each slice was stimulated 40 and 90 min after the onset of superfusion (S_1 , S_2 , duration 2 or 6 min; Fig. 1). Slices superfused with physiological salt solution were stimulated by an electrical field (13 mA; rectangular pulses) generated between two platinum ring electrodes, and slices superfused with Ca^{2+} -free, K^+ -rich solution were stimulated by introduction of 0.65 mM CaCl_2 . In the experiments with somatostatin, the peptide was present from 25 min before S_2 until the end of the experiments. The radioactivity in the superfusates and slices was determined by liquid scintillation counting. All details of the methods used and the calculation of stimulated ^3H overflow above basal efflux have been described previously^{11,12}. The electrically or CaCl_2 -evoked ^3H overflow (for absolute values, see Table 1) from slices preincubated with a ^3H -labelled monoamine mainly consists of the respective nonmetabolized ^3H -monoamine^{11–14} which is released from the corresponding neurones.

Somatostatin at up to 1 μM did not affect the basal efflux of ^3H -noradrenaline, ^3H -dopamine or ^3H -serotonin. However, at

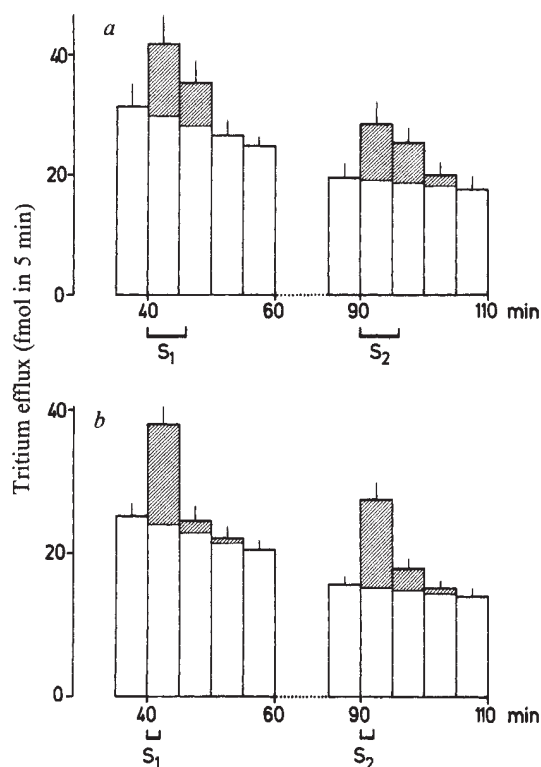


Fig. 1 Tritium efflux from rat hypothalamic slices preincubated with ^3H -noradrenaline (means $\pm$ s.e.m.). The slices were superfused with physiological salt solution of the following composition (mM): NaCl 118, KCl 4.8, CaCl_2 1.3, KH_2PO_4 1.2, MgSO_4 1.2, NaHCO_3 25, ascorbic acid 0.06, disodium EDTA 0.03, glucose 10 (aeration with 95% O_2 and 5% CO_2 ; 37°C). The superfusate was collected in 5-min samples, and the radioactivity was measured by liquid scintillation counting. The slices were stimulated electrically with 360 pulses at frequencies of either 1 Hz (a; $n = 7$) or 3 Hz (b; $n = 7$). Two periods of stimulation were applied, 40 (S_1) and 90 min (S_2) after the onset of superfusion (duration of stimulation indicated by the horizontal bars). The stimulation-evoked ^3H overflow above basal efflux is indicated by the shaded areas of the columns.

Table 1 Stimulation-evoked tritium overflow above basal efflux from superfused rat brain slices preincubated with tritiated monoamines

Slices preincubated with ^3H -noradrenaline		
Tissue (mode of stimulation*)	Tritium overflow	
	fmol	% Of tissue tritium†
Hypothalamus (1 Hz)	17.9 $\pm$ 2.3	1.16 $\pm$ 0.16
Hypothalamus (3 Hz)	15.9 $\pm$ 1.9	1.38 $\pm$ 0.24
Hypothalamus (CaCl_2)	8.6 $\pm$ 1.5	0.40 $\pm$ 0.03
Cortex (3 Hz)	61.6 $\pm$ 10.1	4.35 $\pm$ 1.00

Hypothalamic slices stimulated electrically (3 Hz)*		
Preincubation with	Tritium overflow	
	fmol	% Of tissue tritium†
^3H -dopamine	15.7 $\pm$ 2.8	1.09 $\pm$ 0.18
^3H -serotonin	32.6 $\pm$ 6.8	2.22 $\pm$ 0.44

All values represent tritium overflow evoked by the second period of stimulation (S_2 ; 90 min after onset of superfusion; control experiments; means $\pm$ s.e.m.; $n = 5 - 7$).

* Slices were stimulated either electrically (1 or 3 Hz, 360 pulses, 13 mA; superfusion with physiological salt solution) or by introduction of 0.65 mM CaCl_2 for 6 min after superfusion with Ca^{2+} -free, K^+ -rich solution containing 1 μM tetrodotoxin.

† % of tissue tritium at the onset of the respective stimulation period.

concentrations of 0.32 and 1.0 μM the peptide inhibited electrically (3 Hz, 2 min) induced ^3H -noradrenaline overflow from hypothalamic slices (Table 2). This inhibition was of a similar magnitude when the slices were stimulated at a frequency of 1 Hz for 6 min. Thus, in seven controls the ratio of ^3H overflow evoked by S_2 to that evoked by S_1 (S_2/S_1) was 1.14 ± 0.12 (means $\pm$ s.e.m.), whereas it was 0.84 ± 0.04 ($P < 0.05$, Student's t -test; $n = 7$) when 0.32 μM somatostatin was present from 25 min before S_2 . In contrast, the electrically (3 Hz) induced overflow of ^3H -dopamine or ^3H -serotonin from hypothalamic slices was not altered by somatostatin at up to 1 μM (Table 2). Interestingly, the impulse-evoked ^3H -noradrenaline overflow from cortical slices was also not inhibited by the peptide, although the experimental conditions were identical to those used in hypothalamic slices (see Fig. 1 legend; frequency of stimulation 3 Hz). Thus the ratio S_2/S_1 was 1.04 ± 0.04 ($n = 5$) in control conditions, and 0.96 ± 0.06 (no significant difference) in six experiments with 0.32 μM somatostatin.

Because electrically evoked ^3H -noradrenaline release from brain slices is Ca^{2+} dependent¹², the inhibitory effect of somatostatin on impulse-evoked release from hypothalamic slices may be due to a decrease in the availability of Ca^{2+} ions for stimulus-release coupling. This hypothesis was tested by investigating the effect of somatostatin on ^3H -noradrenaline

Table 2 Effect of somatostatin on electrically evoked tritium overflow from superfused slices of rat hypothalamus preincubated with ^3H -monoamines

Somatostatin (μM)	Tritium overflow (S_2/S_1) after preincubation with		
	^3H -noradrenaline	^3H -dopamine	^3H -serotonin
0	1.12 $\pm$ 0.07	1.05 $\pm$ 0.09	1.00 $\pm$ 0.04
0.1	0.96 $\pm$ 0.03	—	—
0.32	0.77 $\pm$ 0.03*	0.97 $\pm$ 0.05	—
1.0	0.73 $\pm$ 0.08*	1.08 $\pm$ 0.13	0.99 $\pm$ 0.05

The slices were superfused with physiological salt solution. Tritium overflow was stimulated twice, after 40 (S_1) and 90 min (S_2) of superfusion (3 Hz, 2 min), and the ratio of the overflow (above basal ^3H efflux; expressed as % of tissue tritium at the onset of stimulation) evoked by S_2 and that evoked by S_1 was determined (S_2/S_1 ; means $\pm$ s.e.m.; $n = 5 - 7$). Somatostatin was present from 25 min before S_2 until the end of the experiments.

* $P < 0.005$ (compared with the experiments without somatostatin).

release from hypothalamic slices evoked by the introduction of 0.65 mM Ca^{2+} after superfusion with Ca^{2+} -free solution containing 25 mM K^{+} and $1 \mu\text{M}$ tetrodotoxin throughout the experiments. This Ca^{2+} -induced ^3H overflow is due to Ca^{2+} influx into the noradrenergic fibres via the potential-sensitive permeability channel of the cell membrane¹¹. In five control experiments, the ratio S_2/S_1 was 1.18 ± 0.18 , decreasing to 0.63 ± 0.14 ($n = 5$; $P < 0.05$) when $0.32 \mu\text{M}$ somatostatin was present from 25 min before S_2 until the end of the experiments.

In conclusion, the present investigation revealed that somatostatin selectively inhibits the stimulated release of ^3H -noradrenaline from noradrenergic nerve fibres of the hypothalamus, leaving that from cerebral cortex and also the release of ^3H -dopamine and ^3H -serotonin from hypothalamus unaffected. The terminal fibres of central noradrenergic neurones are known to possess various presynaptic

receptors^{12,15,16} which modulate release by modifying Ca^{2+} influx via the potential-sensitive permeability channel¹⁷. Therefore, it is possible that presynaptic somatostatin receptors exist on the noradrenergic fibres of the hypothalamus. The presynaptic site of action seems likely, because the effect of somatostatin was also observed in the presence of tetrodotoxin (which inhibits the propagation of action potentials by decreasing the Na^{+} permeability of the cell membrane), thus excluding the possibility that interneurons are involved in this effect. Our experiments in which Ca^{2+} ions were used for stimulation revealed that the inhibition is probably due to a decrease in Ca^{2+} influx into the terminal noradrenergic fibres.

I thank Miss B. Giesen and Miss G. Werthmann for technical assistance and Serono for the gift of cyclic somatostatin. This study was supported by the Deutsche Forschungsgemeinschaft.

Received 14 July; accepted 18 August 1980.

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Met-enkephalin-Arg⁶-Phe⁷, present in high amounts in brain of rat, cattle and man, is an opioid agonist

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The enkephalins Met-enkephalin and Leu-enkephalin were first isolated from porcine brain by Hughes and co-workers¹. We have recently isolated from bovine adrenals another enkephalin with the structure Tyr-Gly-Gly-Phe-Met-Arg-Phe, or Met-enkephalin-Arg⁶-Phe⁷ (ref. 2). We report here that this new heptapeptide is found in human, rat and bovine striatum in concentrations comparable with or greater than that of Leu-enkephalin. This molecule should not be considered as a mere precursor of Met-enkephalin. A pharmacological study indicates that this naturally occurring enkephalin has similar properties to the two enkephalins characterized earlier.

To demonstrate the presence of this molecule in brain extracts, we used an HPLC system coupled with a radioimmunoassay (RIA) which used an antiserum whose specificity is directed against the N-terminus (Tyr¹-) of the enkephalins. This antiserum reacts as well with Leu-enkephalin as it does with Met-enkephalin. Molecules with a C-terminus deletion (des-Met, Met-enkephalin) or a C-terminus addition (Met-enkephalin-Arg⁶, Met-enkephalin-Lys⁶ and Met-enkephalin-Arg⁶-Phe⁷) also react strongly with this serum (Fig. 1).

HPLC enables all the known enkephalin congeners to be separated in a single run. The system described in Table 1 uses an Ultrasphere octyl column eluted by a gradient of propanol. To detect minute amounts of enkephalins in the eluate we used the RIA described above, which has a sensitivity of 20 pg per tube. The broad specificity of this antiserum is an advantage in that all the characterized enkephalins can be quantified by the same assay.

Table 1 shows that in the striatum and in isolated chromaffin cells Met-enkephalin and Leu-enkephalin were not the only compounds detected by our RIA. We found compounds corresponding to oxidized Met-enkephalin, Met-enkephalin-Arg⁶ and Met-enkephalin-Arg⁶-Phe⁷. Trace amounts of Leu-enkephalin-Arg⁶ (retention time 24 min) and of oxidized Met-enkephalin-Arg⁶-Phe⁷ (retention time 72 min) were also detected.

In all the species examined, Met-enkephalin was always the predominant compound. This contrasts with a report from Simantov and Snyder, who have claimed that in cattle, Leu-enkephalin is the predominant peptide³. To ensure that our relatively lower values for Leu-enkephalin were not due to our RIA procedure, we have confirmed these values with two other assays, a RIA specific for the C-terminus of Leu-enkephalin and a radioreceptor assay^{4,5}.

Compared with values for Met-enkephalin, the amount of Met-enkephalin-Arg⁶ was important in man and rat but not in cattle, a species difference which we cannot explain. This compound has also been isolated from porcine hypothalamus by another group who have called the molecule a pro-Met-enkephalin⁶.

The relative amount of oxidized Met-enkephalin was quite high in human and bovine extracts but not in the rat extracts. The possibility that the oxidation of Met-enkephalin had occurred after death or before or during the preparation of the extracts with 10% trichloroacetic acid, cannot be ruled out.

Met-enkephalin-Arg⁶-Phe⁷ was found in high amounts in the three species examined. In rat and human striatal extracts the concentration was higher than that of Leu-enkephalin. This is seen particularly in the human extract, which contained four times more Met-enkephalin-Arg⁶-Phe⁷ than Leu-enkephalin. This very high ratio of Met-enkephalin-Arg⁶-Phe⁷ to Leu-enkephalin was also found in chromaffin cells isolated from the bovine adrenal medulla.

The presence of this compound in high amounts in all species examined raises some questions about its role in the brain. We have recently reported that this molecule has analgesic activity when administered intraventricularly to mice. On a molar basis, Met-enkephalin-Arg⁶-Phe⁷, with an ED₅₀ of 38.5 nmol per mouse, was 8 times more potent than Met-enkephalin in the tail flick test but 63 times less potent than morphine⁷. However, it

Table 1 Enkephalin congeners in striatum of rat, cattle and man and in isolated chromaffin cells

Retention time on HPLC (min)	Compound	Striatum			Isolated bovine chromaffin cells (ng per 10 ⁶ cells)
		Rat	Cattle	Human	
5	Oxidized Met-enkephalin	2.0	26.0	9.3	0.88
13	Met-enkephalin-Arg ⁶	83.0	5.0	8.6	0.63
19	Met-enkephalin	220.0	450.0	28.0	2.22
45	Leu-enkephalin	30.0	38.0	1.6	0.78
75	Met-enkephalin-Arg ⁶ -Phe ⁷	50.0	25.0	7.5	2.50

Striata from 10 rats (Sprague-Dawley, 200 g) were dissected out and frozen immediately after decapitation. Striata from three bovine brains were obtained in the 3 h following death. The human tissue was obtained at autopsy, 8 h after death, from a 68-yr old woman who died from a pulmonary embolism. In this case only the two putamens were used. Isolated bovine chromaffin cells were prepared as described by Livett *et al.*¹⁰. In all cases the pooled tissues were incubated for 10 min at 95 °C in 10 vol of 1 M acetic acid before homogenization as described in ref. 11. The supernatant (3,000g × 30 min) was precipitated with 10% final trichloroacetic acid, the precipitate was discarded and the solution extracted three times with an equal volume of diethyl ether. The solution was adjusted to pH 4 with pyridine and applied to an Ultrasphere octyl column (5 µm, 4.6 × 250 mm). The column was eluted by a linear gradient of 1-propanol (from 7 to 14% in 100 min) in 0.5 M formic acid/0.4 M pyridine as described elsewhere¹². Flow rate was 30 ml h⁻¹. Fractions of 0.75 ml were collected. After evaporation, the residue was resuspended in the RIA buffer and assayed as described in Fig. 1 legend. Positive fractions were reassayed at two or three appropriate dilutions.

Table 2 Inhibition of binding to rat brain membranes

Peptide	³ H-etorphine	³ H-(D-Ala ²)-Leu-enkephalinamide
	IC ₅₀ (nM)	IC ₅₀ (nM)
Met-enkephalin	25 ± 6 (3)	17 ± 2 (3)
Met-enkephalin-Arg ⁶ -Phe ⁷	35 ± 2 (3)	36 ± 8 (3)
Leu-enkephalin	51 ± 10 (3)	35 ± 3 (3)

Rat brain minus the cerebellum was homogenized with a Teflon-glass homogenizer (1,500 r.p.m., 5 strokes) in 10 ml of 0.05 M Tris-HCl buffer pH 7.4, centrifuged at 49,000g for 10 min, the pellet rehomogenized in 10 ml of Tris buffer and re-centrifuged. The pellet was resuspended in Tris buffer to obtain a final concentration of 1 mg per ml. The suspension (0.8 ml) was incubated for 150 min at 0 °C in the presence of either ³H-etorphine (1 nM) or ³H-(D-Ala²)-Leu-enkephalinamide (3.5 nM) and unlabelled peptides. Nonspecific binding was determined with 1 µM levorphanol for ³H-etorphine and 1 µM (D-Ala²)-Leu-enkephalinamide for ³H-(D-Ala²)-Leu-enkephalinamide as described in ref. 13. The values are the means ± s.e.m.; the number of observations is given in parentheses.

Table 3 Inhibition of contraction of guinea pig ileum (g.p.i.) and mouse vas deferens (m.v.d.)

Compound	Guinea pig ileum	Mouse vas deferens	Ratio IC ₅₀ g.p.i./m.v.d.
	IC ₅₀ (nM)	IC ₅₀ (nM)	
Morphine	80 ± 12 (4)	417 ± 75 (4)	0.19
Met-enkephalin	219 ± 29 (3)	68 ± 6 (3)	3.22
Met-enkephalin-Arg ⁶ -Phe ⁷	322 ± 52 (3)	67 ± 14 (3)	4.81
Leu-enkephalin	601 ± 18 (3)	42 ± 4 (3)	14.3

Assays were performed as described in ref. 13. The values are means ± s.e.m.; the number of observations is given in parentheses.

was possible that the analgesic effect of the heptapeptide was due to its biotransformation. Indeed, *in vitro* Met-enkephalin-Arg⁶-Phe⁷ can be converted to Met-enkephalin by a sequential digestion with trypsin and carboxypeptidase B. To eliminate this possibility we have characterized the new compound in conditions where biotransformation should not occur.

To minimize any enzymatic transformation in our radioligand displacement assay, we have used washed rat brain membranes and incubated them at 0 °C. As Table 2 shows, Met-enkephalin-Arg⁶-Phe⁷ was as potent as Leu-enkephalin in displacing ³H-etorphine or ³H-(D-Ala²)-Leu-enkephalinamide from the purified rat brain membranes. The heptapeptide was slightly less active than Met-enkephalin.

We further characterized the new compound on two classical preparations for opiates, the guinea pig ileum and the mouse vas deferens⁸. On the guinea pig ileum, Met-enkephalin-Arg⁶-Phe⁷ inhibited the electrically induced twitch with an IC₅₀ of 322 nM.

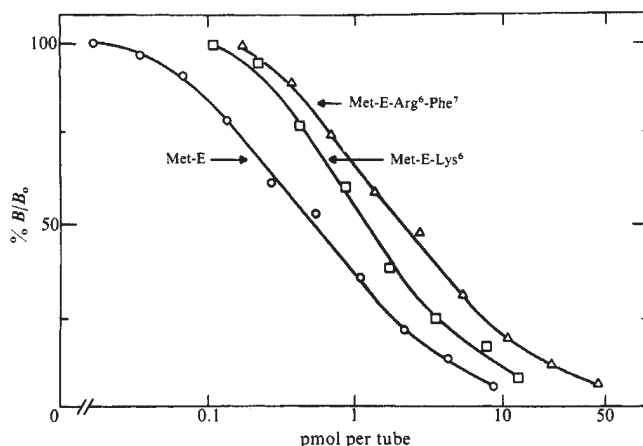


Fig. 1 Cross-reactivities of the N-terminus Met-enkephalin (E) antiserum. A rabbit was injected intradermally at multiple sites with 2 mg of the immunogen emulsified in Freund's complete adjuvant. A month after the first injection it was boosted and serum collected 10 days later. The immunogen was prepared as follows: 40 mg of crystalline bovine serum albumin and 76 mg of 1-ethyl-3-(3-dimethyl-aminopropyl)-carbodiimide HCl were dissolved in 2 ml water. The pH was adjusted to 3. After 4 min in an ice bath, 57 mg of Boc-Met-enkephalin-NH-(CH₂)₂-NH₂ pre-dissolved in 4 ml was added. After 1 h the resulting milky solution was dialysed and lyophilized. The powder was treated with trifluoroacetic acid for 15 min. The trifluoroacetic acid was pumped off under high vacuum, and the resulting brown gelatinous precipitate resuspended in 30% acetic acid/water and dialysed against water. The RIAs were carried out at a final serum dilution of 1/600. The maximum binding was 21%. Serum, trace and standard were incubated for 48 h at 4 °C in a final volume of 300 µl of a 10 mM sodium phosphate buffer pH 7.5, 145 mM NaCl, supplemented with thimerosal 0.01%, gelatine 0.1% and crystalline bovine serum albumin 0.01%. Trace was monoiodo-(¹²⁵I)-Leu-enkephalin prepared as described in ref. 4 and purified by HPLC. Similar results were obtained with monoiodo-(¹²⁵I)-Met-enkephalin. γ-Globulins were precipitated with 0.5 ml of a preparation of formalin-treated *Staphylococcus aureus* after an incubation of 10 min at room temperature. This preparation (Ig Sorb, Enzyme Center, Boston) was diluted 20 times with phosphated-buffered saline before use. After centrifugation (2,000g × 10 min) the supernatant was discarded and the pellet counted. Results are in % of B/B₀. Expressed in molar ratio, the cross-reactivities relative to Met-enkephalin were 100% with sulphoxide Met-enkephalin and Leu-enkephalin, 42% with Met-enkephalin-Lys⁶, 30% with Tyr-Gly-Gly-Phe, 23% with Met-enkephalin-Arg⁶-Phe⁷, 19% with Met-enkephalin-Arg⁶, 1.5% with γ-endorphin, 0.75% with α-endorphin, 0.25% with β-endorphin and 0.20% with δ-endorphin. Parallelism was found for all these compounds except for Met-enkephalin-Lys⁶. No cross-reactivity was found with morphine, tyrosine, des-Tyr¹-β-endorphin or β-lipotropin tested at concentration up to 1 µg per tube.

On this preparation Met-enkephalin was slightly more active and Leu-enkephalin 50% less active. These effects were almost completely antagonized by naloxone (5×10^{-7} M).

Kosterlitz and co-workers have demonstrated the existence of at least two types of opiate receptor— μ and δ in the guinea pig ileum and mouse vas deferens, respectively^{8,9}. Leu-enkephalin was considered to be a δ agonist, being much more potent on the vas deferens than on the guinea pig ileum. On the other hand, morphine was considered to be a μ agonist, being much more potent on the guinea pig ileum than in the vas deferens. In our preparations the ratios of the activity on the guinea pig ileum to that on the mouse vas deferens were 0.19 for morphine and 14.3 for Leu-enkephalin (Table 3). Met-enkephalin-Arg⁶-Phe⁷ had a ratio of 4.81 against 3.22 for Met-enkephalin. Kosterlitz *et al.*⁹ recently showed that compounds with high ratios interacted mainly with δ receptors. Thus, it seems reasonable to consider that the new heptapeptide binds preferentially to the δ receptor rather than to the μ receptor.

Received 28 July; accepted 10 September 1980.

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Met-, Leu-enkephalin and β -endorphin have previously been considered as the main endogenous opioid ligands in the brain. Our report shows that Met-enkephalin-Arg⁶-Phe⁷ is another important endogenous opioid peptide. The crucial problem now is to determine by immunocytochemistry whether or not this compound is present in neurones containing Met- or Leu-enkephalin.

We thank Drs J. Pablo Huidobro-Toro, Sadao Kimura, Randolph Lewis, Stanley Stein, Alvin Stern and Jean-Jacques Vanderhaeghen for their help. J.R. is Chargé de Recherche INSERM (France).

Note added in proof: The analgesic properties of the heptapeptide were markedly enhanced by preparing an analogue more resistant to degradation by peptidases. This compound (D-Ala²)-Met-enkephalin-Arg⁶-Phe⁷-NH₂ was, on a molar basis, 130 times more potent than the natural compound and twice as potent than morphine when administered intraventricularly to mice.

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Development of virus non-producer lymphosarcomas in pet cats exposed to FeLV

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Naturally occurring oncoviruses of several species^{1–6} are transmitted contagiously and cause lymphosarcoma (LSA) or leukaemia in their hosts⁷. All naturally occurring oncoviruses replicate *in vivo* in the tumours they induce or, as with bovine leukaemia virus, can be isolated from tumour cells grown in short-term cell culture^{7,8}. However, we have shown that feline leukaemia virus (FeLV) is not present in a significant minority of pet cats that develop LSA^{9–11}. Unlike experimentally induced virus-negative leukaemias and sarcomas of other species, LSA cells from FeLV-negative LSA cats lack any FeLV proteins, including p15 or p12, and complete functional copies of FeLV provirus and thus do not produce FeLV when grown in cell culture^{4,9–19}. Thus, except for FeLV, the naturally occurring animal leukaemogenic oncoviruses seem to induce only virus-producing lymphoid tumours. Our earlier findings prompted a study to determine the frequency of occurrence of FeLV non-producer (NP) LSA in pet cats and whether NP LSAs develop in cats exposed to FeLV. We report here epidemiological data which indicate that development of NP LSAs in pet cats is associated with exposure to FeLV and suggest that FeLV may be the aetiological agent for FeLV NP feline LSAs. Thus, feline NP LSAs may be suitable for studying the potential viral aetiology and mechanism of leukaemogenesis of human lymphoid tumours in which no oncoviruses have, as yet, been proved to cause the disease.

The FeLV status of most cats with LSA was determined by the immunofluorescent antibody (IFA) test for FeLV performed on

peripheral blood leukocytes using a multivalent rabbit anti-FeLV serum which detects FeLV gp70, p30, p15, and p12 (ref. 17); but an immunodiffusion test⁹, tissue culture isolation⁹, and radioimmunoassays (RIAs)¹⁸ were also done to determine the FeLV status of some cats. The presence of RD114 viral proteins was determined by RIAs of LSA cell lysates¹⁹. In general, the results of the IFA test for FeLV correlated well with all other immunological tests and with tissue culture isolation (Table 1 and refs 9, 11, 13, 17, 19 and 20). We compared the results of the IFA test from 274 cats with our ability to recover infectious FeLV in tissue culture from these cats. We could isolate FeLV from only three of the 153 IFA test-negative cats, a 98% concordance between the two methods of FeLV detection. Conversely, FeLV was isolated from 118 of 121 IFA test-positive cats, a 97.5% concordance. Similar results were obtained when we studied cats with LSA. Of the 57 IFA test-positive LSA cats, 56 (98.3% concordance) were found to have FeLV by tissue culture isolation and of the 33 IFA test-negative LSA cats 31 (93.9% concordance) had no FeLV. These results indicate that detection of FeLV antigens by the IFA test is equivalent to the detection of infectious FeLV. Furthermore, the IFA test can detect even the partial FeLV expression that occurs in FeSV-transformed NP mink cells which do not replicate FeLV or FeSV but which express only FeLV p15 and p12 (ref. 21).

We tested 507 LSA cats for the presence of FeLV and 14 LSA cats for the presence of RD114 viral proteins. We found that 360 of the 507 cats tested (71.0%) had FeLV-positive LSAs and 147 (29.0%) had NP LSAs (Table 2). NP LSAs occurred most frequently in cats with the alimentary form of LSA (Table 2). As reported previously, we found that cats with NP LSA were markedly older than cats which developed FeLV-positive LSAs¹⁴. The mean age of cats with NP LSAs was 6.7 yr; and the median age was 7 yr. In contrast, the mean age of the cats with FeLV-positive LSA was 2.9 yr; and their median age was only 2 yr. Nine FeLV-positive LSAs were tested by RIA and were found to contain large quantities of FeLV structural proteins (Table 1), whereas nine NP LSAs were found to have no detectable FeLV gp70, p30, p15, or p12. However, as reported previously¹⁴, both the FeLV-positive and NP LSAs had low levels of RD114 gp70 (21–22 ng per mg protein) and p15 (34–36 ng per mg protein) whereas FeLV-positive and -negative normal lymphoid tissues had no detectable RD114 antigens (Table 1).

Table 1 Expression of feline leukaemia and RD114 viral antigens and the feline oncornavirus-associated cell membrane antigen (FOCMA) in normal and lymphosarcoma tissues of pet cats

Diagnosis	No. of cats tested	FeLV* status	FOCMA† status	RIA competition assay‡: average viral antigen expression (ng competitor per mg total protein)					
				FeLV antigen expression				RD114 antigen expression	
				gp70	p30	p15	p12	gp70	p15
Normal lymphoid cells	4	—	—	<10	<5	<5	<5	<10	<5
Normal lymphoid cells	2	+	—	ND	1084	259	321	<10	<5
Lymphosarcoma (FeLV non-producers)	9	—	+	<10	<5	<5	<5	21	34
Lymphosarcoma (FeLV producers)	9	+	+	483	859	304	463	22	36

* Determined by the fixed-cell IFA test¹⁷.† Determined by the viable cell membrane IFA test^{13,19}.‡ RIA competition assays were performed as described in ref. 30 with 5 ng of ¹²⁵I-labelled purified viral protein and a limiting amount of specific antibody diluted to the point of ~50% precipitation of the labelled protein. Competition with protein from detergent-lysed cells was quantified by comparison with a standard competition curve with known amounts of purified unlabelled viral protein corresponding to the ¹²⁵I-labelled protein and expressed as the amount required to give 50% reduction in labelled protein precipitation³⁰.**Table 2** Occurrence of feline leukaemia virus in naturally occurring lymphosarcomas of pet cats

Gross form of lymphosarcoma	No. of cats tested	Per cent of cases	No. FeLV positive	Per cent FeLV-positive LSA	No. FeLV-negative	Per cent FeLV non-producer LSA
Multicentric	198	39.1	159	80.3	39	19.7
Thymic	174	34.3	134	77.0	40	23.0
Alimentary	69	13.6	16	23.2	53	76.8
Unclassified	13	2.6	5	38.5	8	61.5
Form unknown	53	10.4	46	86.8	7	13.2
Total	507*	100	360	71.0	147	29.0

* All pet cats with lymphosarcoma were histologically confirmed clinical cases and were examined by W.D.H. or E.G.M. at the Henry Bergh Memorial Hospital of the ASPCA or the Animal Medical Center in New York City.

Table 3 Occurrence of lymphosarcoma in FeLV-exposed and unexposed pet cats

Cat exposure history	Observation years based on:	No. of cats	FeLV status	Observation years		Observed cases of lymphosarcoma		No. of LSAs developing per cat observation year
				Total	Average per cat	FeLV+	FeLV-	
Never exposed	Ages of cats	1,074	1,074 —	3,235	3.1	0	0†	0
Exposed	From time of FeLV exposure*	538	149+ 389—	2,334	4.3	30	11†	0.018
	Total cats	1,612						

* The observation periods for both FeLV-unexposed control cats and FeLV-infected and -uninfected exposed cats were determined in the following ways. For the unexposed FeLV-uninfected control cats the observation period was the age of the cat on the date of its last FeLV test. The observation periods for the exposed cats was the period between the date of the first positive FeLV test of any cat in the household and the termination of this study. The total number of cat observation years for the unexposed and exposed cats was calculated by adding the individual observation periods of all cats in each group. The observation periods for the exposed and unexposed groups of cats were not the same as the exposed cats because the exposed cats had not been exposed for their entire life. To ensure that the difference in the observation periods did not bias our results, we also calculated the observation period for exposed cats in the same way as we did for the unexposed cats—according to their age. In this analysis there was a total of 558 cats, the additional 20 cats were cats that died before our study began and had not been tested for FeLV. The 558 cats were observed for their entire lives for a total observation period of 3,199 yr (an average of 5.7 yr—range 1–24 yr). We found 56 cases of LSA among these 558 exposed cats (30 FeLV-positive, 11 NP LSA and 15 whose status was unknown). The development of LSA per cat observation year was found to be the same (0.018 case) when the observation period was calculated from either (1) the time of FeLV exposure (41 cases of LSA per 2,334 cat observation years = 0.018), or (2) the ages of the cats (56 cases of LSA per 3,199 cat observation years = 0.017). Thus, the difference between the two methods of determining the observation period of the unexposed and exposed tested cats did not alter the conclusion of this study.

† $P < 0.001$.

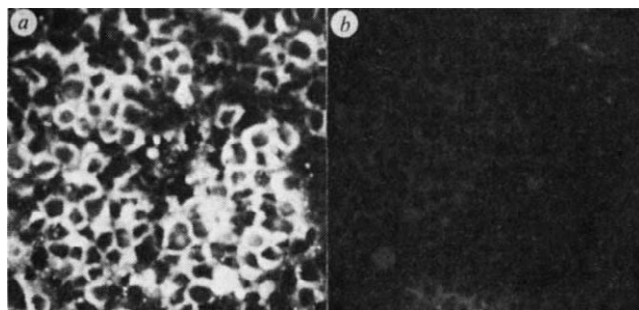


Fig. 1 Examination of feline lymphosarcoma cells for FeLV antigens by the fixed-cell indirect IFA test. The test was done with a multivalent rabbit antiserum against disrupted FeLV that had known reactivity to FeLV gp70, p30, p15 and p12 antigens. *a*, Strong cytoplasmic fluorescence indicates presence of FeLV, but *b*, no such fluorescence is seen in NP LSA cells. Thus the NP LSA cells are devoid of replicating FeLV and FeLV gp70, p30, p15 and p12 expression.

A total of 1,612 FeLV-exposed and unexposed pet cats from all regions of the US were observed for the development of LSA (Table 3). A cat was classified as unexposed if the cat was FeLV-negative and if, according to the owner, the cat had not lived with any FeLV test-positive cat or with any cat which had an FeLV disease. The FeLV status of all cats was determined by the IFA test for FeLV antigens¹⁷. Of the 1,612 cats, 1,074 living in 96 households had never been exposed to FeLV and were uninfected with FeLV. These cats served as controls and were observed for a total of 3,235 cat observation years (an average of 3.1 yr per cat). None of the unexposed control cats developed LSA during this study. In contrast, the remaining 538 pet cats living in 23 households had been exposed to an FeLV-infected cat (Table 3). All of these exposed cats were tested for FeLV and 389 were found to be uninfected whereas 149 were infected. These cats were observed for a total of 2,334 cat observation years (an average of 4.3 yr per cat with a range of 1 to 6 yr) and 41 of these cats developed LSA; 30 of these LSAs were FeLV-positive and 11 were NP LSAs. The difference in the occurrence of NP LSA between the unexposed control cats and the exposed cats is highly significant by the χ^2 test, $P < 0.001$. In one household where there were four unrelated cats, one cat was infected with FeLV and died of FeLV-induced anaemia. What made the household unique was that all three uninfected cats died of NP alimentary LSA.

As infectious FeLV particles, FeLV antigens, and complete copies of FeLV provirus cannot be detected in feline NP LSAs by electron microscopy⁹, tissue culture isolation^{4,9,17}, immunofluorescence (Fig. 1)^{4,17}, RIA^{10,14,19}, or by nucleic acid hybridization^{14,15,16}, the aetiological role of FeLV in these tumours has been uncertain. In contrast to FeLV NP LSA cells, virtually all other oncovirus-transformed cells including FeSV- and MSV-transformed NP fibroblasts, Abelson MuLV and the acute avian leukaemia virus-transformed fibroblasts or leukaemia cells and bovine leukaemia cells are positive for at least the N-terminal viral gag protein by RIA even though they are negative for replicating virus²². We have recently reported that the FeLV-associated tumour-specific antigen, the feline oncornavirus-associated cell membrane antigen (FOCMA), is present on the surface of all FeLV- and FeSV-transformed, virus-producing cat cells, but not on non-transformed virus-producing cat cells. We found that FOCMA is also present on FeLV NP LSA cells suggesting that FeLV may play a role in the transformation of normal lymphocytes into NP LSA cells^{13,22,23}. Our finding that there is a comparable epidemiological association between FeLV exposure and the development of both NP- and FeLV-positive LSAs (Koch's postulates have been fulfilled for the FeLV-positive LSAs)²⁴ supports the hypothesis

that FeLV may be the aetiological agent for most feline LSAs regardless of whether or not they express FeLV.

At least three possible hypotheses explain the mechanism by which a replicating oncovirus such as FeLV causes NP feline LSAs²⁵. First, FeLV may be involved in the generation of a recombinant replication-defective leukaemogenic virus from cat cellular genes and FeLV provirus, similar to the Abelson MuLV, AK-T8 mink cell focus-inducing virus and several avian oncoviruses, although in these NP tumours some viral gag gene expression is present²⁶⁻²⁸. Second, only a fragment of the FeLV genome may be present as provirus in leukaemic cell chromosomes. If such a fragment was present, it would presumably be unable to code for the production of any detectable viral structural proteins, but may be able to initiate transformation²⁹. Third, a 'hit and run' phenomenon might occur in which FeLV alters, but does not stably integrate into the chromosomes of the leukaemic cell.

Feline NP LSA is the only known example of a naturally occurring lymphoid tumour which develops after exposure to a leukaemogenic virus but in which no evidence of that leukaemogenic virus remains. NP LSAs may thus be valuable for the study of the basic mechanism by which viruses, chemicals or radiation induce transformation.

We thank R. Markovich, T. Paino and H. Perry for technical assistance, and Ms S. Passe for statistical analysis. We thank numerous practicing veterinarians and cat owners, especially Mrs S. Bernard, for assistance, and the National Veterinary Laboratory of Franklin Lakes, New Jersey for performing tests for FeLV and helping to obtain cats with FeLV non-producer lymphosarcomas. We also thank Drs Robert Gallo, Nancy Gutensohn and Peter Besmer for helpful discussions. This work was supported in part by grants and contracts from the NCI, The Cancer Research Institute, and the American Cancer Society. During this study W. D. H. was a Scholar and H. W. S. is a Special Fellow of the Leukemia Society of America.

Received 12 May; accepted 29 August 1980.

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Interferon inhibits transformation by murine sarcoma viruses before integration of provirus

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Neoplastic transformation by C-type retroviruses requires synthesis of a DNA copy (the provirus) of the RNA genome and its integration into the host cell DNA. We have previously shown that interferon (IFN) can stably prevent transformation of murine fibroblasts by the Kirsten strain of murine sarcoma virus (KiMSV)^{1,2}, a murine leukaemia virus (MLV). A series of cell clones (IFN clones), isolated in the presence of IFN (10^4 U ml⁻¹) from cultures of NIH-3T3 cells which had been treated with IFN, and then infected with KiMSV (KiMLV) in conditions where every cell was infected, were shown to be phenotypically untransformed. These untransformed cells did not produce virus or contain rescuable KiMSV. However, cells isolated using an identical procedure, but in the absence of IFN, were uniformly transformed and all produced KiMSV (KiMLV) or contained rescuable KiMSV^{2,3}. It was concluded that IFN either prevents synthesis or integration of the provirus, or else that in the presence of IFN the provirus is integrated such that it is not expressed. We now show that five representative clones contain no detectable KiMSV proviral DNA, and also that the initial stages of infection by KiMSV (KiMLV) are inhibited by IFN treatment. IFN seems to act before integration, preventing either the synthesis or the integration of proviral DNA.

We initially sought to establish whether the IFN clones contained integrated KiMSV provirus in their cellular genomes, by hybridizing cell DNA with a representative ³H-cDNA probe synthesized from purified KiMSV (KiMLV) RNA. As normal uninfected mouse DNA contains multiple copies of endogenous retrovirus sequences closely related to MLV genomes⁴, it was necessary to reduce the proportion of KiMLV cDNA sequences in the probe by annealing with KiMLV RNA. After this procedure the cDNA hybridized to a maximum level of about 16% with KiMLV RNA and 78% with KiMSV (KiMLV) RNA. It was then used as a cDNA probe for hybridization with various cell DNAs. The results (Table 1) show that there was some annealing of the cDNA probe with the DNA from uninfected NIH-3T3 cells, reflecting the inefficiency of the selection procedure, and that a much higher level of hybridization (~58%) occurred between the cDNA probe and the DNA from a non-producer, transformed cell line, CCI, which is known to contain a rescuable KiMSV genome.³ The level of hybridization with DNA from the IFN clones was no higher than that seen with DNA from uninfected cells, strongly suggesting that the IFN clone DNAs do not contain integrated KiMSV proviral DNA.

The cell DNAs were further investigated for the presence of integrated provirus by restriction enzyme analysis using the Southern blotting procedure. Figure 1A shows the restriction map of unintegrated linear KiMSV DNA using endonuclease *Pst*I (details of the restriction mapping will be presented elsewhere). *Pst*I analysis of a number of KiMSV-transformed non-producer cell DNAs has shown each to contain the two large internal fragments *P*₁ (molecular weight 2.6×10^6) and *P*₂ (molecular weight 1.05×10^6) (Fig. 1A). These two internal *Pst*I fragments (representing 80% of the KiMSV genome) therefore provided a means of detecting integrated provirus. *Pst*I-digested cell DNAs were electrophoresed on an agarose gel and the fragments transferred to a filter which was then annealed with KiMSV (KiMLV) ³²P-cDNA to give the result shown in Fig. 1B.

Lane a shows the hybridization of the cDNA with the MLV-related sequences of uninfected cell DNA. In lane b, which contains a digest of CCI DNA, the two internal *Pst*I fragments (arrowed) are clearly visible against the background of hybridization. However, these fragments are absent from the IFN clone DNAs (c-g) showing that intact integrated provirus was not present. The use of other restriction enzymes, which cleave once or twice within the provirus, confirmed that no KiMSV-specific fragments were detectable in the IFN clone DNAs (data not shown).

Thus, we conclude that cells infected in the presence of IFN do not contain complete integrated proviral genomes and are unlikely to contain truncated forms of proviral DNA. IFN must therefore prevent transformation by KiMSV at a stage before integration.

The possibility that IFN was acting by inhibiting adsorption or penetration of the virus was investigated by determining the effect on KiMSV (KiMLV) transformation of IFN added after infection. Transformation was assayed by focus formation on monolayer cultures of C3H10T $\frac{1}{2}$ cells; the virus stock used contained an excess of KiMSV and focus formation using this stock at high dilution follows one-hit kinetics, that is, a focus is initiated by infection of a cell by KiMSV alone and enlargement of the focus is due to outgrowth from this cell alone rather than by virus spread or recruitment¹. In such conditions, any effects of

Table 1 Hybridization of KiMSV cDNA with cellular DNAs

Source of DNA	% Hybridization	
	Cell DNA	cDNA probe
NIH 3T3	82	19
	78	16
CCI	82	58
	86	57
IFN 49	89	19
	83	16
IFN 81	77	14
	76	15
IFN 85	71	14
	82	10
IFN 61	76	16
	73	14
IFN 91	86	16
	76	15

NIH-3T3 cells and a KiMSV-transformed non-producer line, CCI, were grown as described previously³. Details of the isolation of the IFN clones (IFN 49, 61, 81, 85 and 91) are given by Morris and Burke². Cell DNAs were prepared by deproteinization with phenol/chloroform (1:1, v/v), spooling under ethanol (EtOH), RNase A digestion (50 µg ml⁻¹ for 1 h at 37 °C), further deproteinization, ether extraction and spooling under EtOH. The high molecular weight DNA was dissolved in 10⁻³ M EDTA and sheared by sonication. Virion RNA (35S) was prepared from a purified KiMLV preparation containing excess KiMSV and used as a template for the *in vitro* synthesis of ³H-cDNA by AMV reverse transcriptase essentially as described by Taylor *et al.*⁵. The reaction mixture contained 50 mM Tris pH 8.3, 40 mM KCl, 8 mM MgCl₂, 5 µg calf thymus DNA primer, 100 µCi ³H-TTP (42 Ci mmol⁻¹), 0.2 mM dATP, dGTP, dCTP, 0.5 mM dithiothreitol, 4 mM Na pyrophosphate, 0.5 µg RNA and 7.5 units of AMV reverse transcriptase in a volume of 50 µl. Incubation was for 1 h at 37 °C. cDNA was purified by phenol/chloroform extraction, EtOH precipitation, alkali hydrolysis, a second EtOH precipitation, Sephadex G-100 chromatography and further EtOH precipitation. The cDNA was then selected by self-annealing and annealing with poly(rA) to remove anticomplementary (+ strand) sequences and oligo(dT) polymers, and annealed with KiMSV (KiMLV) RNA (at a ratio of 1:5 RNA:cDNA) to produce a representative cDNA probe. At this ratio 90% of the RNA hybridized to DNA. Finally the cDNA was hybridized with a 100-fold excess of KiMLV RNA to reduce the proportion of KiMLV cDNA sequences which can anneal with mouse DNA. Hybridizations were carried out in 2.4 M phosphate buffer (PB) (1.2 M Na₂HPO₄, 1.2 M NaH₂PO₄ pH 7.0) at 76 °C. These conditions, devised by D. E. Kohne (La Jolla Cancer Research Foundation), give a reproducible stimulation of the rate of hybridization (D. E. Kohne, personal communication). The cDNA was annealed with cell DNA, with the latter in at least 5 × 10⁶-fold excess, ensuring that a single integrated provirus would be in at least fivefold excess over the cDNA. The extent of hybridization with cDNA and reassociation of cell DNA (demonstrating the validity of each hybridization experiment) were determined by retention on hydroxyapatite in 0.14 M PB at 61 °C.

IFN are due to an influence on the initial transformation event or on growth of transformed cells, rather than to effects on virus spread¹. Murine C-type viruses penetrate and uncoat rapidly (within 80 min in NIH-3T3 cells at 37 °C)¹¹, whereas at least 3 h are required for the antiviral effect of IFN to develop (ref. 12 and A.G.M., unpublished data). Thus, the addition of IFN to cells after their infection would be expected to have very little effect on transformation if its effects were exerted at this early stage. However, it was found that IFN added as much as 4 h after infection was virtually as effective at blocking transformation as pretreatment with IFN (Table 2). Even when added as late as 24 h post infection, IFN still inhibited focus formation to some extent (Tables 2 and 3) indicating that, in some infected cells, the IFN-sensitive stage was not complete. However, in reconstruction experiments treatment with IFN for 24 h had no effect on focus formation by cells stably transformed by KiMSV (KiMLV) and producing KiMSV (KiMLV) (data not shown),

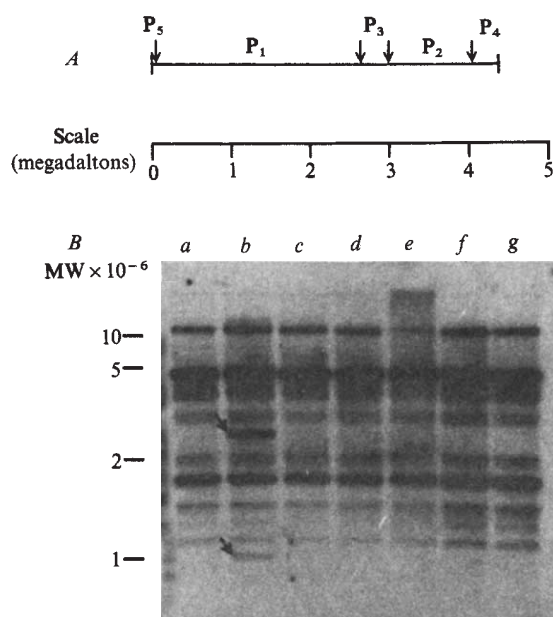


Fig. 1 *A*, Restriction endonuclease cleavage map of unintegrated linear KiMSV DNA. *B*, Hybridization of KiMSV (KiMLV) cDNA with endonuclease *Pst*I fragments of cell DNAs. High molecular weight DNA was prepared as described in Table 1 legend and 10-μg samples were cleaved with an excess of endonuclease *Pst*I (Boehringer) and then run on a 1.0% agarose horizontal slab gel. DNA fragments were denatured *in situ* and transferred to a nitrocellulose filter (BA 85, Schleicher and Schuell) by the method of Southern⁶. For hybridization, a ³²P-labelled cDNA was synthesized as for the ³H-cDNA probe (Table 1) except that pyrophosphate was omitted and actinomycin D (100 μg ml⁻¹) was included in the reaction mixture to suppress (+) strand cDNA synthesis⁷ and ³H-TTP was replaced by unlabelled TTP and dCTP by 125 μCi [α-³²P]dCTP (350 Ci mmol⁻¹). The ³²P-cDNA was purified as described for the ³H-cDNA (Table 1) and used without further selection. The filter was annealed with 2.5 × 10⁶ c.p.m. of ³²P-cDNA in a volume of 2.0 ml in a sealed polythene bag for 60 h using hybridization conditions described by Shank *et al.*⁸. Unlabelled KiMLV RNA (5.0 μg ml⁻¹) was included in the hybridization medium to suppress the level of background hybridization of cDNA with KiMLV-related sequences present in mouse DNA. After annealing, the filter was washed⁸ and treated with RNase A (10 μg ml⁻¹) in 15 mM NaCl, 1.5 mM Na₃ citrate at 37 °C for 20 min. The filter was exposed to X-ray film (Fuji RX) at -70 °C for 1 week using a Dupont Cronex 'Lightning Plus' intensifying screen. *a*, Uninfected NIH-3T3 DNA; *b*, CCI DNA; *c*-*g*, DNA from IFN clones², IFN 49, 61, 81, 85 and 91 respectively. Molecular weights of restriction fragments were determined using *Eco*RI⁹ and *Hind*III¹⁰ fragments of bacteriophage λ DNA as size markers.

Table 2 Effect of IFN treatment before and after infection with KiMSV (KiMLV)

Time of IFN addition (h)	Mean no. of foci per plate
-24	0.5
+1	0
+2	1.0
+4	0
+6	2.5
+24	10.5
None	13.25

IFN (10⁴ U ml⁻¹ and 2 × 10⁸ U mg⁻¹) was added to cultures of C3H10T^{1/2} cells at the times indicated and removed 24 h later. All cultures were infected with 30 FFU of KiMSV (KiMLV) at 0 h. Transformed foci were scored 10 days later.

Table 3 Effect of IFN treatment on KiMSV (KiMLV) infection of serum-deprived cells

Period of serum deprivation (h)	Period of IFN treatment (h)	Mean no. of foci per culture
None	None	27
-24 to 264	None	0
None	-24 to 0	0
None	24 to 48	10.5
-24 to 72	None	12
-24 to 72	24 to 48	0

Cultures of C3H10T^{1/2} cells¹³, otherwise maintained in medium containing 5% serum, were shifted into medium containing 0.25% serum (serum deprivation) and treated with IFN (10⁴ U ml⁻¹) for periods as indicated. All cultures were infected at 0 h with KiMSV (KiMLV) at 30 FFU per culture. Transformed foci were scored 10 days later.

showing that the effect was not due to an inhibition of growth of transformed cells. These data indicated that IFN probably does not act by inhibiting adsorption, penetration or uncoating of the virus.

An extension of this experimental approach suggested that IFN acts at or after provirus synthesis. In cells arrested in G₀ by serum deprivation, C-type virus replication is blocked^{14,15}. It seems that in such conditions synthesis of proviral DNA begins but is not completed and integration does not occur. Cultures of normal mouse fibroblasts (C3H10T^{1/2}) were blocked in G₀ by prolonged serum deprivation and then infected with KiMSV (MLV) (30 FFU (focus-forming units) per culture). Addition of serum 48 h later allowed transformation (again scored by focus formation), showing the block to be reversible. However, when IFN was added 24 h post infection, so that it is present for the 24-h period before serum addition, transformation was essentially completely prevented (Table 3). A similar IFN treatment of cells which had not been serum deprived was much less effective in preventing transformation. This suggests that IFN acts at, or later than the stage blocked by serum deprivation.

It therefore seems that IFN can block infection by C-type viruses at a stage after uncoating but before integration of the provirus. This is not due to the cell growth inhibitory effect of IFN as in these and other experiments IFN had no significant effect on the growth of the cells used; nor is it likely to be an effect of IFN on translation of viral mRNA, as translation of input genomic RNA is probably not significant in the virus life cycle¹⁶⁻¹⁸.

This effect of IFN is at least superficially similar to the Fv-1 restriction phenomenon¹⁹⁻²¹ in which the Fv-1 gene product appears to prevent integration of proviral DNA; it may be that here IFN is acting in a way that is analogous to the effect of the Fv-1 gene product.

This work was supported by grants from the Cancer Research Campaign.

Received 28 July; accepted 17 September 1980.

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Heterogeneity of poly(I).poly(C)-induced human fibroblast interferon mRNA species

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Three classes of human interferons (IFNs) have been defined on the basis of their immunological properties: the 'Le' or ' α ' IFN, mainly derived from leukocyte or lymphoblastoid cells; the 'F' or ' β ' IFN, mainly derived from fibroblast cultures; and the 'T', 'immune' or ' γ ' IFN, mainly derived from mitogen- or antigen-stimulated lymphoid cells¹. Whereas several individual species of Le IFN have been purified to homogeneity^{2–4}, it is generally considered that F IFN represents a single protein^{5,6}. Thus current efforts to clone human fibroblast IFN mRNA sequences are based on the observation that F IFN mRNA sediments in sucrose gradients as a single RNA species of size corresponding to 12–14 S (refs 7–10). We show here, using gel electrophoresis of mRNA, that two populations of translationally active human fibroblast IFN mRNA molecules exist—an abundant '14 S' species and a scarce '11 S' species. Microinjection of either species of mRNA into *Xenopus* oocytes leads to the synthesis of biologically active F-type human IFN. These data agree with and complement recent RNA hybridization studies of Weissenbach *et al.*¹⁰.

Polyadenylated IFN mRNA was prepared from diploid human fibroblast cultures (FS-4 strain) exposed to poly(I).poly(C) and cycloheximide for 4 h as described earlier^{7,11}. In some experiments the induced cells were fractionated using hypotonic swelling and Dounce homogenization^{7,11} and cytoplasmic polyadenylated RNA was prepared. Appropriate amounts of IFN mRNA preparations were mixed with ³²P-labelled HeLa cytoplasmic RNA, the samples made 6 M in urea, heated at 95 °C for 2 min, cooled rapidly in an ice bath and electrophoresed through a cylindrical agarose–6 M urea gel^{12,13}. Adjacent slices in the appropriate region of the gel were pooled, the RNA eluted and assayed for IFN mRNA activity by microinjection in oocytes of *Xenopus laevis*. Figure 1a shows the electrophoretic profile of translationally active IFN mRNA in preparations of cellular polyadenylated RNA from induced FS-4 cells. Figure 1b shows a similar profile of IFN mRNA in preparations of cytoplasmic polyadenylated RNA. At least two populations of IFN mRNA are clearly resolved in each

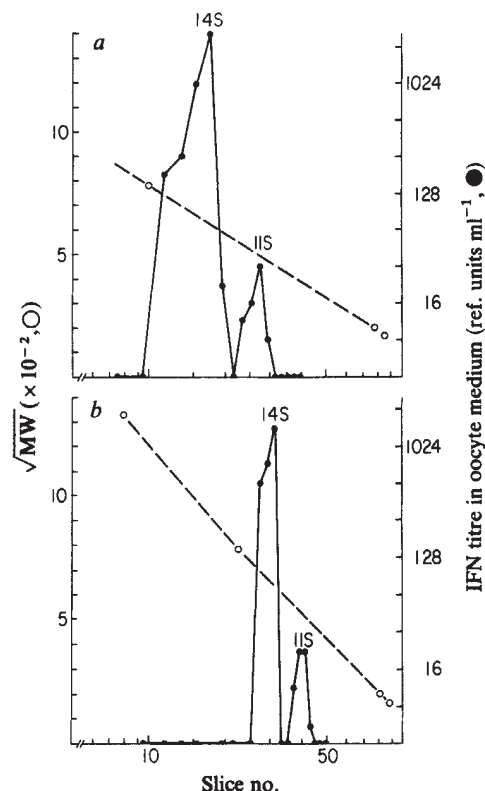


Fig. 1 Electrophoresis of human fibroblast IFN mRNA preparations through agarose–6 M urea gels. Polyadenylated RNA preparations obtained from FS-4 cultures induced with poly(I).poly(C) (30 μ g ml⁻¹, P.-L. Biochemicals) and cycloheximide (50 μ g ml⁻¹, Calbiochem) for 4 h were mixed with an appropriate amount of ³²P-labelled HeLa cell cytoplasmic RNA in 50 μ l distilled water. The samples were made 6 M in urea (Eastman or Schwarz-Mann) and 50 mM in NaCl, and 5 μ l glycerol saturated with bromophenol blue was added. The samples were then heated at 95 °C for 2 min, cooled rapidly in an ice bath and electrophoresed through a 2.5% (a) or 2% (b) agarose (Biorad)–6 M urea cylindrical gel (0.6 $\times$ 11 cm) in half-strength Loening's buffer (Tris-HCl 0.02 M, sodium acetate 0.01 M, EDTA 0.001 M, pH 7.8) at 4 °C and 5–6 mA per tube ($\sim$ 8 V cm⁻¹) using the modified¹³ procedure of Locker¹². After electrophoresis, the gels were sliced manually into 1-mm slices and the ³²P content of each slice monitored by Cerenkov counting to locate the positions of 28 S, 18 S, 5 S and 4 S marker RNA species (O). The MWs for marker RNA species were taken to be 1.75 $\times$ 10⁶, 0.605 $\times$ 10⁶, 3.9 $\times$ 10⁴ and 2.6 $\times$ 10⁴ for 28 S, 18 S, 5 S and 4 S RNA species, respectively²⁹. Adjacent slices in the appropriate regions of the gel were pooled (2 slices per pool) and the RNA eluted as described elsewhere¹³. The RNA recovery was in the 50–80% range as estimated by the recovery of ³²P-labelled RNA present in each slice. Each RNA pellet was washed with 2 M LiCl and then with ethanol, dried and dissolved either in 2 μ l (a) or in 5 μ l (b) sterile distilled water. A 2- μ l aliquot of each RNA sample was microinjected into 15–20 oocytes of *X. laevis* and the oocytes incubated in 0.2 ml Barth's medium for $\sim$ 40 h^{11,30}. The IFN content (●) of the oocyte incubation medium (ref. 31; P.B.S., in preparation) was estimated by a semi-microassay on GM258, GM2767 or FS-4 cells with VSV as the challenge virus^{32,33}. All IFN titres are expressed in terms of the 69/19 reference standard for human IFN. a, Cellular polyadenylated RNA (37 μ g) electrophoresed through a 2.5% agarose–6 M urea gel. b, Cytoplasmic polyadenylated RNA (30 μ g) electrophoresed through a 2% agarose–6 M urea gel.

case: an abundant species of length 1,100–1,200 residues (corresponding to a sedimentation value of 14 S using the relationship $MW/330 = \text{number of residues} = 4.7 S^{2.1}$) and a less abundant species of length 700–800 residues (corresponding to a sedimentation value of 11 S). For convenience we refer to these two species of mRNA as the '14 S' and '11 S' IFN mRNAs.

In the experiment illustrated in Fig. 1b only 40% of each RNA sample eluted from gel slices was assayed in oocytes. The remaining 60% of RNA corresponding to the individual 14 S and 11 S species was denatured once more and electrophoresed individually through another agarose-urea gel. The second set of gels was then sliced and appropriate gel slices assayed for IFN mRNA activity. Both the 14 S and 11 S species re-electrophoresed as RNA corresponding to 14 S and 11 S respectively (data not shown).

We have electrophoresed a sample of IFN mRNA through an agarose- CH_3HgOH gel^{14–17} in fully denaturing conditions (10 mM CH_3HgOH). Figure 2 indicates that the two populations of IFN mRNA can also be resolved when RNA electrophoresis is carried out in stringent denaturing conditions. Whereas a 1.75% agarose gel was used in the experiment illustrated in Fig. 2, we now routinely use a 2% agarose gel. In these conditions the abundant species is of length 1.3 kilobases (six determinations, ± 40 residues, s.e. of mean), whereas the less abundant species is of length 0.9 kilobases (six determinations, ± 40 residues).

The translation product of the 14 S and 11 S mRNA species has been characterized as the human F-type IFN (Table 1). The antiviral activity synthesized by *Xenopus* oocytes in response to

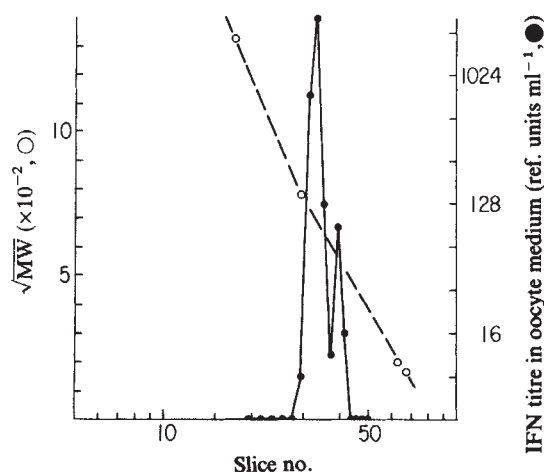


Fig. 2 Electrophoresis of a human fibroblast IFN mRNA preparation through an agarose- CH_3HgOH gel. Cellular polyadenylated RNA (45 μg) obtained from induced FS-4 cells was mixed with ^{32}P -labelled marker RNA and was made 10 mM in CH_3HgOH (stock 1.27 M, Alfa Division, Ventron) in half-strength borate buffer (full strength corresponds to: 0.1 M boric acid, 6 mM sodium borate, 1 mM EDTA, 10 mM sodium sulphate, pH 8.2) in a total volume of 50 μl and was allowed to stand for 5 min at room temperature. 5 μl of glycerol saturated with bromophenol blue was then added and the RNA electrophoresed through a 1.75% agarose-10 mM CH_3HgOH cylindrical gel ($0.6 \times 11 \text{ cm}$) in borate buffer at room temperature (4 mA per tube; 3.5 V cm^{-1}) until the dye was close to the bottom of the tube gel (5 h; ref. 17). After electrophoresis the gel was placed in 100 ml of a solution containing 100 mM β -mercaptoethanol and 0.01 M Tris-HCl, pH 7.4, for 40 min on a rotary shaker at room temperature. The gel was then sliced manually, the locations of marker RNA (O) monitored by Cerenkov counting, RNA in appropriate regions of the gel eluted (the elution buffer contained 1 mM dithiothreitol¹³), dissolved in 2 μl distilled water and assayed for IFN mRNA activity (●) as indicated in Fig. 1 legend.

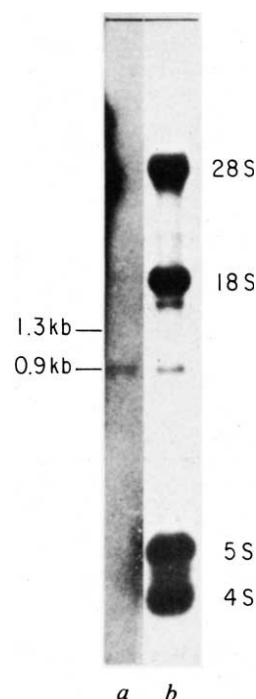


Fig. 3 Hybridization analysis of human fibroblast IFN mRNA species using ^{32}P -labelled *Pst*I/*Bgl*II fragment of the IFN cDNA insert in clone TpIF319-13. Cellular polyadenylated RNA (12 μg) obtained from induced FS-4 cells was glyoxylated in 50% dimethylsulphoxide at 50°C for 45 min, electrophoresed through a 1.5% agarose slab gel in 10 mM sodium phosphate buffer (pH 6.5) until the bromophenol blue dye had moved $\sim 15 \text{ cm}$ from the origin. ^{32}P -labelled HeLa cytoplasmic RNA was also glyoxylated and electrophoresed in an adjacent slot in the gel. After electrophoresis the RNA was transferred to APT-paper and hybridized as described by Alwine *et al.*³⁴ ^{32}P -labelled *Pst*I/*Bgl*II DNA fragment of clone TpIF319-13 (1.7×10^5 Cerenkov c.p.m.) was heat-denatured (65°C for 10 min in 50% formamide) and hybridized to the RNA-containing paper in 1 ml of hybridization buffer (50% formamide, 0.75 M NaCl, 0.075 M sodium citrate, 1X Denhardt's solution, 20 mM sodium phosphate buffer, pH 6.5, and 0.2% sodium dodecyl sulphate) for 72 h at 37°C . The hybridized DNA was detected by autoradiography. The presence of the 0.9- and 1.3-kilobase translatable IFN mRNA species in the mRNA preparation used in this experiment was verified using the procedure in Fig. 2 legend. Lane a, IFN mRNA preparation; lane b, ^{32}P -labelled HeLa cytoplasmic RNA. kb, Kilobases.

microinjection with individual 14 S and 11 S mRNA species is completely neutralized by anti-F IFN antiserum but is largely unaffected by anti-Le IFN antiserum.

The results presented here are directly relevant to the interpretation of recent data obtained using cloned human fibroblast IFN mRNA sequences^{8–10,18}. Weissenbach *et al.*¹⁰ have described plasmids containing cDNA inserts (in pBR322) derived from polyadenylated RNA extracted from poly(I).poly(C)-induced human diploid fibroblasts (FS-11 strain). DNA from one of these clones (clone A341), which has been identified as an 'interferon' clone, hybridizes to two populations of polyadenylated RNA from induced cells: an RNA of length 1,100–1,200 residues hybridizes strongly to this DNA probe whereas another species of length ~ 750 residues hybridizes weakly. Their data do not allow one to determine whether the two populations of RNA function as translationally active IFN mRNA species as sucrose gradient sedimentation analysis by these investigators reveals a single peak of biologically active IFN mRNA sedimenting at 12–14 S (corresponding to a length of 1,100–1,200 residues). The enhanced resolution of gel electrophoretic analyses of IFN mRNA described here clearly

Table 1 Neutralization of IFNs synthesized by *Xenopus* oocytes in response to microinjection with separated 14 S and 11 S mRNA species

Expt	mRNA	Residual IFN titre (ref. units ml ⁻¹) after mixing with anti-IFN antiserum			
		No antiserum	Anti-F	Anti-F and anti-Le	Anti-Le
1	11 S	256	<8	Not done	128
	14 S	192	<8	Not done	128
2	11 S	1,280	<10	<10	640
	14 S	160	<10	<10	80
3	14 S	120	<10	<10	120
Antiserum controls					
Fibroblast IFN		512	<2	<2	256
Leukocyte IFN		2,408	1,024	<16	<16

RNA recovered from gel slices corresponding to the peaks of 14 S and 11 S IFN mRNA as described in Fig. 1a was injected into groups of oocytes (20–30 per group), which were then incubated in 0.2 ml Barth's medium for 30–40 h at room temperature. The clarified oocyte homogenate was used to set up neutralization assays²⁸. Briefly, 100- μ l aliquots of a 1:4 or 1:5 dilution of the oocyte homogenate in cell culture medium (Eagle's minimal essential medium containing heat-inactivated fetal bovine serum, 10% v/v) was mixed with 2 μ l (expts 2, 3 and control IFN preparations or 10 μ l (expt 1) anti-F IFN antiserum (batch 2 + 282) or 10 μ l of a 1:10 dilution of anti-Le IFN antiserum (batch 903) or both. Controls free of antiserum were mixed with an appropriate volume of culture medium. The samples were incubated for 60–90 min at 37 °C and serial twofold dilutions (50- or 100- μ l aliquots) of each sample were added to confluent, 1-day-old monolayers of human GM258 cells in multiwell microtitre dishes. The cultures were incubated for 20–24 h at 37 °C, the IFN- and antiserum-containing medium was removed and replaced with fresh culture medium containing vesicular stomatitis virus (VSV). The residual IFN titre represents the reciprocal of the highest dilution of the original oocyte homogenate that protected GM258 cell monolayers and is expressed in terms of the 69/19 reference standard for human IFN. Fibroblast IFN used to test the specificity of the antisera was prepared by superinduction of FS-4 cell cultures with poly(I)·poly(C), cycloheximide and actinomycin D³³, whereas the leukocyte IFN used was prepared by induction of human peripheral blood buffy coat preparations with Sendai virus.

demonstrates that both populations of RNA represent translationally active mRNA species for human F-type IFN.

Human fibroblast IFN mRNA sequences have also been cloned by a group of Japanese investigators^{8,9,18}. The DNA restriction map and nucleotide sequence obtained by Taniguchi *et al.* (clone TpIF319-13, ref. 18) is different from that for clone A341 (M. Revel and M. Zeevi, personal communication). Therefore it seemed likely that clone A341 would correspond to the 1.3-kilobase IFN mRNA and that clone TpIF319-13 would correspond to the 0.9-kilobase mRNA species. Figure 3 presents a test of this hypothesis. Polyadenylated RNA obtained from induced FS-4 cells was denatured by glyoxylation, electrophoresed in a 1.5% agarose slab gel, transferred to APT-paper and hybridized to ³²P-labelled, nick-translated, 359-base pair, *Pst*I/*Bgl*II DNA fragment of the cDNA insert in clone TpIF319-13. This DNA fragment corresponds to the middle and carboxy-terminal portions of the human fibroblast IFN coding sequence. It can be seen from Fig. 3 that this probe hybridized exclusively to an RNA species of approximate length 0.9 kilobase. Thus the 1.3-kilobase fibroblast IFN mRNA has a sequence which is substantially different from that of clone TpIF319-13.

Although we have resolved two size classes of human F IFN mRNA by electrophoresis in agarose gels, we cannot exclude further sequence heterogeneity within each size class.

Data on the effect of glycosylation inhibitors on the physical properties of fibroblast IFN synthesized in their presence (ref. 19; Y. K. Yip and J. Vilček, personal communication) as well as recent protein fractionation studies (refs 20, 21; E. Knight Jr,

personal communication) suggest the existence of more than one human F-type IFN protein. This heterogeneity may reflect the existence of distinct chromosomal genes for fibroblast IFN such as on human chromosome 2 or 5 or 9 (refs 22, 23). Alternatively, the heterogeneity may arise from the existence of alternative pathways for processing the primary transcript of IFN gene(s) in the cell nucleus.

The existence of multiple species of human leukocyte (Le)-type human IFNs as well as of murine IFNs has been clearly demonstrated^{2-4,24,25}. Furthermore, recent nucleic acid cloning experiments demonstrate the existence of at least two distinct sequences for human Le IFN^{26,27}. Gel electrophoretic analyses of IFN mRNA species from these sources may be highly instructive. It is likely that IFN genes constitute a large multi-genic family of inducible genes which code for cellular proteins with antiviral, anticellular and immunomodulatory effects in eukaryotic cells.

This investigation was partly stimulated by a seminar given by Dr Michel Revel at The Rockefeller University on 18 February 1980. We thank Dr T. Taniguchi for the ³²P-labelled *Pst*I/*Bgl*II DNA fragment of clone TpIF319-13 and Mr Benjamin Neel for assistance in carrying out the blot-hybridization experiment. We also thank Drs I. Tamm, J. Vilček, E. A. Havell, E. Knight and M. Zeevi for helpful discussions, Drs J. Vilček and E. A. Havell for the anti-IFN antisera, Dr W. E. Stewart II for a sample of human Le IFN and Drs T. Taniguchi, M. Revel and K. Cantell for preprints. We thank Mr Ira Augenzucker for technical assistance. This investigation was supported by NIAID, DHEW grant AI-16262. P.B.S. is the recipient of a Junior Faculty Research Award from the American Cancer Society.

Note added in proof: In accordance with current guidelines for interferon nomenclature [*Nature* 286, 110 (1980)], we suggest that the translation product of the 0.9-kilobase IFN mRNA (Fig. 2) be designated human interferon- β_1 and that of the 1.3-kilobase IFN mRNA be designated human interferon- β_2 .

Received 9 April; accepted 26 August 1980.

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Interferon-dependent induction of mRNA activity for (2'-5')oligo-isoadenylate synthetase

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At least three different enzymes involved in the regulation of protein synthesis are induced in a variety of cells by interferon (IFN)¹⁻⁵. Sensitive assays for these enzymes have been developed and used to establish the specificity, dose dependence and time course of their induction by IFN⁵⁻⁸. One of these enzymes, the oligo-isoadenylate synthetase E, whose product (2'-5')pppApApA⁹ activates the latent ribonuclease F¹⁰⁻¹¹, is increased over 50-fold after IFN treatment. We describe here the assay for an mRNA from IFN-treated mouse L cells, that produces oligo-isoadenylate synthetase activity when injected into *Xenopus* oocytes. This mRNA is found in the cells only after exposure to IFN. The mRNA increases in mouse L cells with the same time course as the enzyme activity itself. In particular, there is a 3-h lag period between IFN addition and the onset of enzyme and mRNA accumulation. Using anti-IFN antibodies, we show that during this lag period the continued interaction of IFN with the cells is necessary for the full induction of the oligo-isoadenylate synthetase.

Poly(A)-containing RNAs¹² were prepared from cytoplasmic extracts of L929 monolayer cultures which had been exposed for different times to 200 U ml⁻¹ mouse IFN⁵. The RNAs were injected into *Xenopus laevis* oocytes¹³, extracts from these oocytes were added to poly(rI)·(rC)-agarose beads, which were then incubated with [α -³²P]ATP to measure the synthesis of (2'-5')oligo-isoadenylate as previously described⁵. In parallel, the cellular level of the oligo-isoadenylate synthetase was measured in the NP40 cytoplasmic extracts from the same cultures (Fig. 1a). Formation of the phosphatase-resistant (2'-5')(Ap)_nA oligonucleotides is only seen with extracts from IFN-treated cells. Figure 1b (lane 1) shows that extracts of *Xenopus* oocytes do not normally form any (2'-5')ApA by themselves (see also ref. 6), but (2'-5')ApA synthesis appeared clearly in extracts of oocytes injected with poly(A)⁺-mRNA from IFN-treated cells (lane 4). Identification of this activity in injected oocytes, with the IFN-induced oligo-isoadenylate synthetase, is based on the following arguments: (1) Formation of the (2'-5')ApA results from an enzymatic activity which binds to the poly(rI)·(rC)-agarose beads, no significant activity being detected without this purification step. (2) The activity appears only if mRNA from IFN-treated cells is injected into the oocytes (compare lanes 2 and 4 in Fig. 1). (3) The phosphatase-treated products, labelled with [α -³²P]ATP, co-migrated in several thin-layer chromatography and electrophoresis systems^{9,10}, with chemically synthesized (2'-5')ApA markers. The predominance of dimers in the oocyte products is due to the low level of enzyme used; the same is found when a limited reaction is carried out with purified synthetase¹⁰. (4) Finally, the products of a large-scale reaction (with 1 ml oocyte extract instead of the 0.02 ml routinely used) inhibited Mengo RNA translation in L-cell extracts (Table 1) proving that biologically active (2'-5')oligo(A) is formed. In these conditions (2'-5')oligo trimers were seen by electrophoresis of the phosphatase-treated products (not shown). No translational inhibition was found with the products of mRNA from cells not treated with IFN.

In conditions where (2'-5')oligo(A) synthesis is proportional to the amount of extract used, we compared the oligo-iso-

adenylate synthetase activity in L cells and in mRNA-injected oocytes (Table 1, right). The enzyme activity produced in oocytes by injection of mRNA from L cells treated for 8 h with IFN represents ~1% of the enzyme activity present in the same volume of cell extract from which the mRNA was prepared. We verified that untreated-cell mRNA, which does not yield synthetase activity, is not inhibitory in our assay: 33,400 c.p.m. (2'-5')ApA were formed with extracts of oocytes injected with 1 μ g of 8h-mRNA, against 3,600 c.p.m. for 0h-mRNA, and 45,100 c.p.m. for the mixture of 0h- and 8h-mRNA. The accumulation of oligo-isoadenylate synthetase in L cells exposed to IFN is, therefore, accompanied by a proportional increase in an mRNA yielding this enzymatic activity in the oocyte assay. In similar experiments, we have found that exposure of human lymphoblastoid Namalva cells to leukocyte

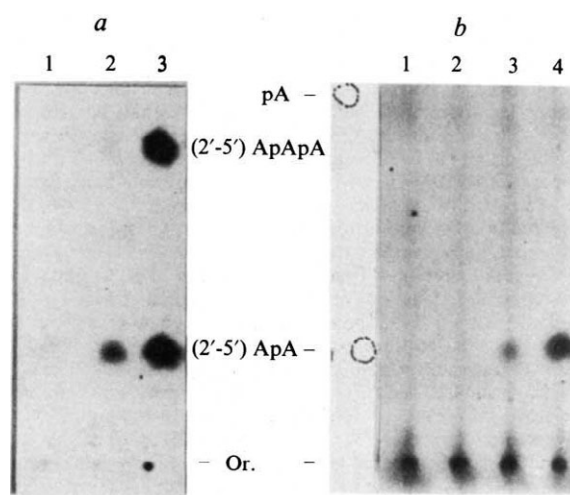


Fig. 1 Formation of active oligo-isoadenylate synthetase by translation of IFN-induced mRNA in *Xenopus* oocytes. L929 monolayer cultures in minimal Eagle's medium with 8% calf serum were exposed for 0, 3 or 8 h at 37 °C to 200 U ml⁻¹ mouse IFN (induced in L cells by Newcastle disease virus and purified at 10⁷ U per mg protein⁵). Cells from seven plates were washed with 35 mM Tris-HCl pH 7.5, 140 mM KCl, 3 mM Mg acetate and lysed with 0.5% Nonidet P40 (NP40) in 5 mM Tris-HCl pH 7.8, 100 mM NaCl, 3 mM Mg acetate (2 ml per plate). After 30 min, nuclei were removed by centrifugation at 2,000g for 10 min. **a**, Enzyme activity in cell extracts. 20 μ l cytoplasmic extract was mixed with 50 μ l poly(rI)·(rC)-agarose beads (P.L. Biochemicals). After 10 min at 30 °C, unbound proteins were removed by washing the beads twice in 20 mM HEPES buffer pH 7.5, 120 mM KCl, 5 mM MgCl₂, 1 mM dithiothreitol, 10% glycerol (Buffer B). Beads were incubated in 10 μ l of 2.5 mM [α -³²P]ATP (0.24 Ci mmol⁻¹) and 2.5 mM dithiothreitol for 20 h at 30 °C. Beads were centrifuged down, washed with 10 μ l water and the two supernatants combined. 6 μ l were treated with bacterial alkaline phosphatase and subjected to paper electrophoresis at pH 3.5 (4 kV, 3 h) and autoradiography as previously described⁵. Positions of (2'-5')ApA and ApApA were indicated by synthetic markers. Extracts of cells treated 0 h (lane 1), 3 h (lane 2) and 8 h (lane 3) with IFN are shown. **b**, Enzyme synthesized in oocytes. To the cytoplasmic extracts, 3 mM EDTA and 0.5% dodecyl sulphate were added and RNA was extracted three times by 1 vol phenol-chloroform-isoamylalcohol (50:50:1), precipitated with 2 vol ethanol and the poly(A)⁺ sequences was purified on oligo(dT)-cellulose¹². Groups of 10 *Xenopus* oocytes were injected with 50 ng RNA (in 50 nl) per oocyte as described by Gurdon *et al.*¹³. The oocytes were kept in 0.15 ml Barth's medium for 20 h and then homogenized with 0.5 ml Buffer B. Aliquots (20 μ l) of homogenate were used to assay (2'-5')oligo(A) synthesis as above. Lane 1, water-injected oocytes; lanes 2, 3 and 4, oocytes injected with mRNA from L cells, treated 0, 3 and 8 h with IFN, respectively. UV spots of markers are shown. All radioactive spots were cut out and counted by Cerenkoff radiation in a scintillation counter. Results are given in Table 1.

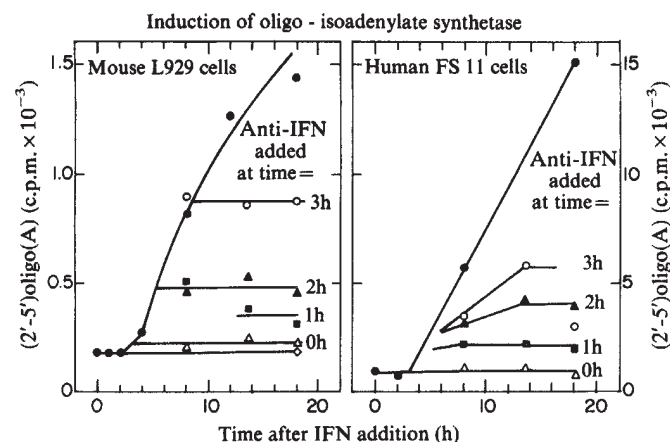


Fig. 2 Delayed effect of anti-IFN antibodies on oligo-isoadenylate synthetase E induction by IFN. Monolayer cultures of mouse L929 or human foreskin FS11 cells (about 3×10^4 cells per well of a 96-well microplate) received 50 U ml⁻¹ mouse L-cell IFN or 15 U ml⁻¹ human fibroblast IFN¹⁹, respectively. The level of enzyme E was measured as before⁵, at the time indicated on the abscissa. Antibodies to mouse L-cell IFN or antiserum to human fibroblast IFN obtained in rabbits¹⁹ were added (at dilutions of 1/100 and 1/20, respectively, see Table 2) at the indicated times after IFN addition. The lower activity of the L cells reflects use of less radioactive ATP in this assay.

IFN also induces mRNA yielding oligo-isoadenylate synthetase activity in the oocyte assay (not shown).

In cell cultures exposed to IFN, induction of the oligo-isoadenylate synthetase does not start immediately on addition of IFN but is preceded by a 2–3-h lag period (ref. 5 and Fig. 2). This lag is characteristic of IFN action and does not depend on the amount of IFN used. With the oocyte assay we compared the level of mRNA activity for the oligo-isoadenylate synthetase, at 3 and 8 h after IFN addition. Although some mRNA activity can be detected at 3 h (Fig. 1b, lane 3), over 90% of the mRNA present at 8 h is formed during the 3–8-h period, whereas less than 10% is made from 0–3 h after IFN addition (Table 1). A more than 10-fold increase in mRNA activity from 3 to 8 h could also be calculated from the translation inhibition experiment shown in Table 1: 50% inhibition was seen at a 1:1,000 dilution for the 3-h mRNA products and at 1:20,000 for the 8-h mRNA products. Like enzyme synthesis, induction of the mRNA seems, therefore, to be a slow process.

This delayed response to IFN prompted us to examine how long IFN has to interact with the cells to trigger oligo-isoadenylate synthetase induction. Antibodies against mouse IFN were added to L-cell cultures to interrupt the action of IFN at different times after its addition. When added together with IFN, the antibodies blocked completely induction of oligo-isoadenylate synthetase, whereas replication of vesicular stomatitis virus (VSV) was able to proceed normally as in the absence of IFN (Table 2). Antibodies, therefore, block the cell response to IFN but do not impair other cell functions such as viral replication. The effect is specific as anti-mouse IFN did not inhibit oligo-isoadenylate synthetase induction by human IFN in human cells and, conversely, anti-human fibroblast IFN did not inhibit the effect of mouse IFN on L cells (Table 2). Figure 2 shows that, in mouse and human cells, the delayed addition of antibodies, at 1, 2 or 3 h after IFN addition, can still interrupt the already initiated process of enzyme induction. Enzyme accumulation starts but stops at a certain level. The enzyme level reached increases with the time between IFN and anti-IFN additions. Thus, when anti-mouse IFN is added to L cells 3 h after IFN, the induction proceeds for 8 h but then stops. Thus, to complete the induction process, IFN has to act for more than 3 h,

that is, beyond the lag period. In human foreskin cells, the kinetics of synthetase induction are somewhat slower than in mouse L cells⁵, and as shown in Fig. 2, the inhibition by delayed addition of antibodies is even more pronounced than in L cells. The antiviral effect of IFN against VSV replication in these cells was also inhibited by antibodies against human IFN, 3 h after IFN addition (not shown).

Antibodies do not penetrate inside living cells¹⁴. The inhibitory effects of anti-IFN added 2 or 3 h after IFN probably results, therefore, from neutralization of IFN molecules still present outside the cell. Although IFN binds rapidly to cells¹⁵, it does not seem to enter the cell rapidly, as already suggested by experiments with antibodies to the chromosome 21-coded human IFN receptor^{16,17}. The lag period in the oligo-isoadenylate synthetase induction could then be explained by a prolonged action of IFN outside the cell, the resistance to neutralization by antibodies developing only just before the enzyme and its mRNA activity measured in the oocyte assay start to accumulate in the cytoplasm of the cells. The parallel increase in translatable mRNA and in enzyme observed in our

Table 1 Induction by interferon of mRNA for oligo-isoadenylate synthetase

Time after IFN addition (h)	Oligo-isoadenylate synthetase activity			
	% Translation inhibition with		³² P-(2'-5')oligo(A) synthesis†	
	products of mRNA-injected oocytes* Dilution		with products of mRNA-injected oocytes (c.p.m.)	with products of L-cell cytoplasmic extracts (c.p.m.)
0	1:250	1:25,000	45 (1)	13,660 (4)
3	87	6	275 (8)	54,170 (17)
8	95	44	3,410 (100)	316,670 (100)

Figures in parentheses are per cent of the 8-h enzyme level.

* Measured by Mengo virus RNA translation in L-cell extracts as in ref. 3. ³⁵S-methionine incorporation without oligonucleotides was 94,500 c.p.m. A background without mRNA of 3,000 c.p.m. was subtracted. The oligonucleotide products from 1 ml oocyte extract were diluted as indicated in the 0.25 ml translation reaction mixture.

† Measured by [α -³²P]ATP incorporation into (2'-5')ApA + ApApA cores with 0.02 ml oocyte extract as in Fig. 1 legend; calculated for 1 μ g poly(A)⁺ mRNA and for the 0.25 ml cytoplasmic extract from which this RNA originates.

Table 2 Use of anti-interferon antibodies to inhibit oligo-isoadenylate synthetase induction

IFN	Antibodies to IFN	Oligo-isoadenylate synthetase ³² P-(2'-5')oligo(A) (c.p.m.)		VSV growth (PFU ml ⁻¹)
		Mouse cells	Human cells	Mouse cells
None	None	1,750	725	4.4×10^{10}
Mouse IFN	None	20,500	—	2×10^5
Mouse IFN	Anti-mouse IFN	2,120	—	4.3×10^{10}
Human IFN	None	—	5,175	—
Human IFN	Anti-mouse IFN	—	5,270	—
None	None	4,610	2,500	—
Mouse IFN	None	32,830	—	—
Mouse IFN	Anti-human IFN	32,055	—	—
Human IFN	None	—	16,100	—
Human IFN	Anti-human IFN	—	2,600	—

IFN and anti-IFN antibodies were added together to the cells, in the conditions described in Fig. 2 legend. The enzyme assay was carried out after 8 h for mouse L929 cells and after 14 h for human foreskin FS11 cells. Where indicated, mouse cells were infected at 8 h with 4 PFU per cell VSV and the virus growth was measured 24 h later. PFU, plaque-forming units.

experiments suggests that the main control of enzyme accumulation is formation of new mRNA. This is consistent with the inhibition of induction by actinomycin D, and by cycloheximide, which also indicates that there is no activation of a preformed enzyme in the cells⁵. We had previously reported⁵ that actinomycin D added 2 h after IFN does not block any more oligo-isoadenylate synthetase induction in L cells: this seems to contradict the more than 10-fold increase in mRNA measured by the oocyte assay from 3 to 8 h after IFN addition. On the other hand, the results obtained by delayed antibody addition are in line with the kinetics of mRNA accumulation. Actinomycin D causes a phenomenon of superinduction⁵, and the normal level of enzyme found when actinomycin D is added at 2 h may reflect a more efficient expression of a smaller amount of mRNA. Actinomycin D cannot, therefore, be easily used to analyse the induction process.

The mRNA assay described here should facilitate the study of the mechanism by which IFN induces oligo-isoadenylate

synthetase, a process tightly correlated with its biological activity^{5,7,8}. An important question still to be solved is whether the mRNA product is the enzyme itself, a regulatory factor or a combination of polypeptides. This question cannot be answered until the polypeptide structure of the enzyme is determined. Farrell *et al.*¹⁸ have described the synthesis of some proteins by translation of IFN-induced mRNAs in reticulocyte lysates, but could not identify any enzymatic activity. The oocyte assay demonstrates for the first time that IFN induces in the cells an mRNA involved in the synthesis of oligo-isoadenylate synthetase.

We acknowledge helpful suggestions from Dr H. Sorek and D. Giveon and the technical assistance of Ms Sara Tzur. Synthetic markers for the assay were given by Dr S. Rapoport and Y. Lapidot, and antibodies to mouse L-cell IFN by Dr G. Galasso. This work was supported by GSF (Israel) and NCRD (München).

Received 28 February; accepted 2 September 1980.

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Transcriptional fidelity of histone genes injected into *Xenopus* oocyte nuclei

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Previous work has indicated that at least some of the genetic information required for the expression of sea urchin histone genes is recognized following injection of the gene repeat (h22) into *Xenopus* oocyte nuclei^{1,2}. The ability to elicit the expression of cloned genes and their sequence-manipulated counterparts is proving invaluable in analysing the molecular details of gene expression^{2,3}. Direct injection of such genes into *Xenopus* oocyte nuclei remains one of the simplest methods for obtaining such expression and a remarkable degree of transcriptional fidelity has been demonstrated using this system with RNA polymerase III genes^{4–9}, and to a lesser extent with rDNAs transcribed by RNA polymerase I^{10,11}. In the case of polymerase II genes there is ample evidence for coupled transcription–translation^{12–14}, but the degree of transcriptional fidelity involved may, as has recently been shown for the ovalbumin gene¹⁵, be minimal. However, clearly if the oocyte is to be used to investigate transcriptional regulation of such genes, transcriptional fidelity defined as the production of correct RNA termini, rather than the production of ‘functional mRNAs’ (ref. 15), must pertain¹⁶. Here we demonstrate such fidelity in the expression of all five *Psammechinus miliaris* histone genes comprising a repeat unit. However, we find large quantitative variations in the levels of synthesis of the individual correct termini and hence of the mRNAs. In addition to the mRNAs, species with no detectable counterparts in the sea urchin are generated off the coding strand, as are heterogeneous noncoding species.

We have previously shown that RNA electrophoretically indistinguishable from authentic H2A and H2B mRNAs is synthesized by polymerase II-transcribing supercoiled micro-

injected histone gene repeats¹. Moreover, the histone DNA must be free of vector DNA¹ because its presence (both in *trans* and in *cis*) is strongly inhibitory. We have also argued that these mRNAs are essentially primary transcripts¹⁷, and thus reflect faithful transcription in the oocyte^{1,2}. Consequently, the lack of high levels of the other mRNAs (H3, H4, H1) implied some transcriptional deficiency such as a lack of fully functional promoters for these genes with respect to the *Xenopus* enzymes. This explanation seemed most probable for the H1 and H4 genes, as they (in contrast to the H3 as well as the H2A and the H2B genes) lack clear versions of the TATAAATA and cap sequence upstream of the structural genes¹⁷.

To test this idea we needed to assay levels of correct promotion (production of 5' termini) independent of termination. We therefore cut the h22 repeat with a combination of restriction enzymes which produced fragments five of which gave suitable overlaps to all the h22 5'-mRNA termini from within the coding sequence (Fig. 1b). As the 5' termini of the mRNAs have been mapped previously¹⁷, the lengths of the overlaps could be predicted and the relative levels of the correct 5' termini in RNA samples visualized by a multi-probe 5' S₁ mapping technique (see Fig. 1 legend). When authentic sea urchin RNA is used with this probe, there are, as predicted, strong bands protected by the 5'-terminal sequences of the five histone mRNAs and with the anticipated sizes (Fig. 1, lane 3). Positive identification of the correspondence of bands to given mRNAs was achieved by mapping partially purified mRNAs with the multiple probe (lanes 4–8, H4, H2B, H3, H2A, H1 mRNAs, respectively). The faint high-molecular-weight bands are due to renatured DNA probe fragments whose labelled ends were not removed by S₁ nuclease because they co-migrate with the input DNA and are observed independently of the RNA (not shown).

These results with authentic sea urchin mRNAs may be compared with the strikingly similar pattern of protected bands observed when h22-injected oocyte RNA is used as the RNA component of the reaction (Fig. 1, lane 2). Bands corresponding to all the correct mRNA 5'-terminal sequences are present, indicating a qualitatively correct promotion of these genes but with relative intensities significantly different from those present in the sea urchin RNA. This is most evident for the H4 5' band which, although relatively very faint, is nevertheless clearly

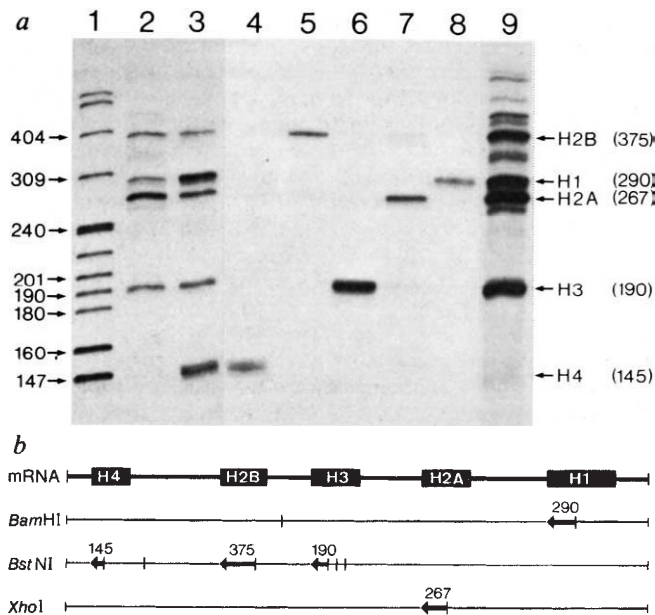


Fig. 1 Multiple-probe S_1 mapping of h22 5' mRNA terminal sequences present in sea urchin-derived RNA or in h22-injected *Xenopus* oocyte RNA. S_1 mapping was carried out essentially as described previously for individual 5' mRNA termini¹⁷, but scaled down to 10 μ l and with a 5' 32 P-labelled, triple restriction digest (*Bam*I, *Bst*NI and *Xho*I) of the h22 repeat DNA as probe. The cognate DNA protected by the histone mRNA 5'-terminal sequences is shown in panel b. The indicated lengths of DNA protection by the individual mRNAs are calculated from previous mapping of the 5' termini and the DNA sequence¹⁷. Note that labelled 5' ends outside the mRNA map cannot be protected from S_1 within a mRNA/DNA hybrid and are even susceptible in DNA duplex because they overhang the 3' termini. a, Lane 1, 32 P-labelled DNA size marker¹⁹; lane 2, 5–14S sucrose gradient-purified h22-injected oocyte RNA from approximately two oocytes each injected with 4 ng of h22 circles and incubated overnight at 18 °C (ref. 20); lane 3, 5 μ g of total RNA from *P. miliaris* embryos at the 128-cell stage of development; lanes 4–8, partially purified *P. miliaris* histone mRNAs²¹, in order H4, H2B, H3, H2A and H1; lane 9, longer exposure of lane 2. Experiments in lanes 2 and 3 and 4–8 were carried out in parallel. Faint high-molecular-weight bands are due to renatured probe (see text). Numbers in parentheses indicate the size in bases.

present with longer exposure (lane 9). The H1 band is also relatively less intense than the H2B, H2A and, surprisingly, the H3 band. We interpret these differences in abundance of 5'-terminal sequences as reflecting differential promotion of the mRNA transcripts^{1,2,17}. The alternative explanation of differential stabilities can be ruled out by our observation that the *de novo* synthesized histone mRNAs are essentially stable in the oocyte (ref. 1 and unpublished data), in apparent contrast to histone mRNAs directly injected into the oocyte cytoplasm¹⁸.

Thus, we also conclude from this experiment that differential transcription of correct histone mRNA 5'-terminal sequences in h22-injected oocyte RNA reflects the differential pattern of expression of the complete mRNAs except in the case of H3 gene, where the high levels of correct H3 5'-terminal sequences are not matched by an equal abundance of the mRNA¹. A deficiency in the production of the correct 3' terminus for this mRNA, presumably as a result of poor termination, could account for this discrepancy. To test this idea and to demonstrate the fidelity in the production of 3' termini by the oocyte, we performed a multiple-probe S_1 mapping similar in concept to that used for the 5' termini but with 3'-end-labelled *Xho*I/*Hpa*II fragments capable of mapping all but the H4 histone mRNA 3'

termini (Fig. 2b). The results using the sea urchin RNA or partially purified individual mRNA are shown in Fig. 2, lanes 3–9. When the h22-injected oocyte RNA is used with this probe (Fig. 2, lane 2), presumptive correct termination is indicated by strong bands corresponding to correct H1, H2A and H2B 3'-terminal sequences, but, as anticipated, only a faint band at the H3 position is observed. In fact, the H3 mRNA 3' terminus seems to be the only mRNA 3' terminus whose production is quantitatively deficient, because in a separate experiment (not shown) we detected H4 mRNA 3'-terminal sequences in an abundance which matched transcripts originating from correct H4 mRNA 5' termini. In contrast, the large imbalance of correct H3 mRNA 5' over 3' termini must be compensated by H3 RNA species with incorrect 3' termini. Further examination of Fig. 2, lane 2 suggests synthesis in the oocyte of RNA species comprising the correct H3 5'-terminal sequences but with long 3' extensions compared with the mRNA. Thus, the input *Hpa*II fragment used to probe the H3 3' region (indicated by a closed arrowhead) is protected from the S_1 to a much greater extent than other input fragments, as is the next fragment transcriptionally downstream (*Hpa*II/*Xho*I; open arrowhead) which

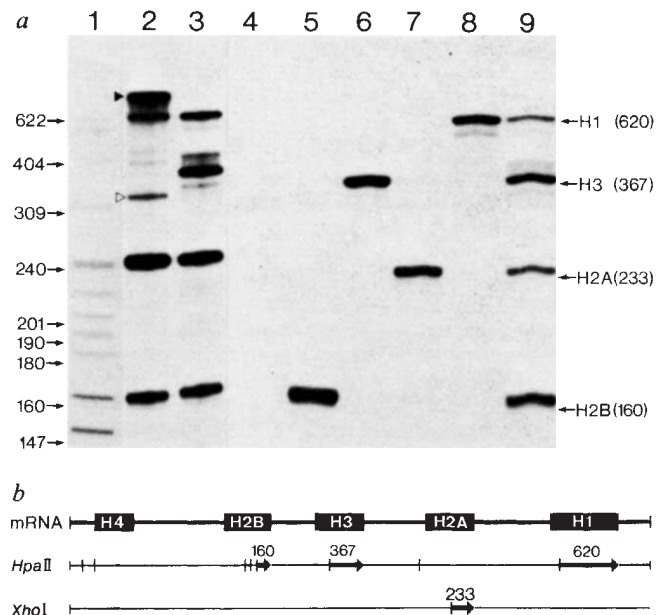


Fig. 2 Multiple-probe S_1 mapping of the h22 3'-terminal sequences of the H2B, H3, H2A and H1 mRNAs present in sea urchin- or h22-injected oocyte RNA. S_1 mapping was as in Fig. 1 legend except that the probe comprised 3' 32 P-end-labelled *Hpa*II/*Xho*I restriction fragments of h22 as shown in panel b. The 3'-end labelling was achieved by filling in recessed 3' ends with highly purified DNA polymerase I²² (from NEN nick-translation system) in the presence of [α - 32 P]dCTP and using the nick-translation protocol of the supplier but without DNase addition and with a reduced incubation period (15 min at 12 °C). A low level of internal labelling nevertheless occurred, causing the background of faint, spurious band with this probe. The indicated lengths of expected DNA protection by the H2B, H3, H2A and H1 mRNA 3'-terminal sequences are calculated from previous mapping of the 3' terminal and from the DNA sequence¹⁷. a, Lane 1, 32 P-labelled DNA size marker¹⁹; lane 2, 5–14S sucrose gradient-purified h22-injected oocyte RNA from approximately two oocytes²⁰; lanes 3 and 9, 5 μ g of total RNA from *P. miliaris* embryos at the 128-cell stage of development; lanes 4–6, partially purified *P. miliaris* histone mRNAs in order H4, H2B, H3, H2A and H1²¹. Note that the H4 3'-terminal sequence is not mapped by this probe because the *Hpa*II site lies just upstream of the mRNA¹⁷. Arrowheads indicating non-mRNA-derived band in lane 2 (oocyte RNA) co-migrate with two specific input DNA fragments and are discussed in the text.

starts in the H3-H2A spacer and ends in the middle of the H2A coding region. Protection of these fragments is not apparent when sea urchin RNA is used (compare lanes 2 and 3). The exact end(s) of the H3 3' extensions cannot be unambiguously deduced from these data but the fact that one can follow specifically protected DNA fragments into the H2A coding region suggests that a significant proportion of the species starting with the correct H3 5' sequence read through to the correct H2A 3' terminus and are thus 'di-cistronic' H3/H2A mRNAs (see below). Evidence of a minor level wholly incorrect termination is revealed by the presence of discrete oocyte RNA-derived bands not present when sea urchin RNA is used (compare lanes 2 and 3).

Taken together, the S_1 mapping data discussed above predict the synthesis in the injected oocyte of all five correct histone

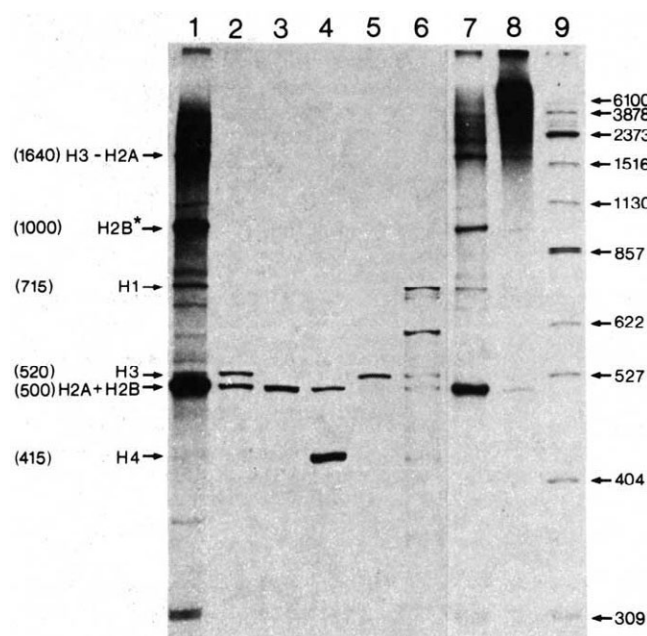


Fig. 3 Strand-selected transcripts of h22 in microinjected oocytes. Lane 1, overexposure of ^{32}P -GTP-labelled coding strand-selected RNA transcripts of h22-injected oocytes. Lane 7 shows normal exposure. h22 strands were separated on alkaline CsCl gradients (density at 4 °C 1.700, 0.1 M NaOH, 6 mM EDTA, 30,000 r.p.m. for 3.5 days in a VT:50 rotor). Recovered single strands were judged to be about 95% pure and were bound to diazobenzylmethyl (DBM) paper²³. Complementary injected oocyte RNA was purified by hybridization in 60% formamide, 0.15 M NaCl, 25 mM phosphate buffer, pH 7.1, and 0.2% SDS at 45 °C for 2–12 h and elution with 90% formamide at 60 °C. RNA was analysed on a 6% acrylamide 8 M urea gel containing 10 mM TBE buffer and 0.2% SDS, and with continuous buffer recirculation. Gels were treated with diphenylloxazole and dried before exposure. Lanes 2–6, ^3H -labelled *P. miliaris* histone mRNAs²¹ further purified with DBM filters loaded with restriction fragments comprising H2B and H3 sequences, H2A sequences, H2A and H4 sequences, H3 sequences and H1 sequences, respectively. Lane 8, noncoding strand-selected h22 transcripts obtained as for coding transcripts (lanes 1 and 7) but by hybridization to noncoding-strand on DBM paper. Note that there are several discrete 'coding' RNA species visible in this lane and similarly some polydisperse RNA is visible in the overexposed coding-strand RNA (lane 1) consistent with cross-contamination of the strands on the DBM filters accentuated by the conditions of local DNA excess in the hybridizations²³. Lane 9, ^{32}P -DNA size marker. The band labelled H2B* is an example of a coding-strand RNA species whose length precludes it comprising both normal 5' and 3' termini (see text). In the hybridization conditions used for strand-selected RNA, essentially no endogenous *Xenopus* transcripts were recovered in control experiments (not shown).

mRNAs, albeit with large quantitative variations, as well as species with correct starts and stops but with readthrough at one or more termination signal (such as an H3/H2A di-cistronic transcript) and species arising from erroneous initiation and/or termination. To verify these predictions, we have analysed the h22-coded oocyte RNA from both coding and noncoding DNA strands on fully denaturing gels as shown in Fig. 3. The RNA species selected by the coding strand (Fig. 3, lane 7) are discrete and include RNA species identifiable by co-migration with authentic mRNAs (Fig. 3, lanes 2–6) as well as by hybridization (not shown) as correct histone mRNAs, with the H2A and H2B mRNAs being abundant, H1 showing an intermediary concentration and with both H3 and H4 mRNAs, whose synthesis is respectively very deficient in the production of correct 3'- and 5'-terminal sequences, being scarce but clearly visible with overexposure (lane 1). An abundant RNA species with the expected length of an H3-H2A di-cistronic mRNA (about 1,640 bases) is present, as are other species in the size range ($\geq 1,700$ bases) expected for di- or even tri-cistronic mRNAs. The presence of an abundant di-cistronic H3-H2A mRNA explains our recent finding (ref. 1 and E.P., unpublished) that, despite the very low levels of correct H3 mRNAs, the H3 protein is synthesized in the oocyte at levels comparable to the H2A and H2B proteins. These large RNA species are not mRNA precursors because they are stable in the oocyte and exit like the mRNAs into the cytoplasm (ref. 1 and unpublished data). In addition, a minor proportion of discrete RNA species are synthesized whose length precludes the possibility that they comprise both normal 5' and 3' mRNA termini. An example is the species H2B* which hybridizes to the H2B region of the repeat. The RNA selected by the noncoding strand (lane 8) is, in contrast, of high molecular weight and polydisperse. Although contributing a significant amount to the total mass of RNA transcripts¹, it presumably arises from relatively infrequent, erroneous promotion and/or termination.

In conclusion, our results show definitely that all five genes of the sea urchin histone repeat are capable of being faithfully transcribed within an amphibian nucleus but with strikingly different efficiencies, generally reflecting the differential rates of promotion but in the case of the H3 gene reflecting defective termination. It will be interesting to know whether analogous experiments with *Strongylocentrotus purpuratus* histone genes¹⁴, or with chicken histone genes (J. Wells, personal communication) yield comparable results.

We thank Mrs S. Oberholzer and Mr F. Ochsenbein for assistance in preparing the manuscript, and K. Gross for providing partially purified mRNAs. This work was supported by a grant from the State of Zürich, by Swiss National Research Foundation grant 3.257.077 and by an EMBO fellowship for C.H.

Received 25 July; accepted 22 September 1980.

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MATTERS ARISING

Peridotite xenoliths in basalts and mantle dynamics

BASU¹ has described jointed and angular xenoliths of mantle peridotite in alkali basalts from California. He considers their morphology to be due to brittle fracture at the site where the xenoliths were incorporated into the rising magma, and thus to be representative of dynamic conditions in the upper mantle. I believe this conclusion to be unwarranted, for the following reasons.

Mitchell *et al.*² have modelled the thermal response of xenoliths to enclosing magma, and have demonstrated that blocks of the size described by Basu are heated to the temperature of their surroundings in a matter of hours. Exceptionally high magma ascent rates are, therefore, required if xenoliths are to be brought from the mantle to the surface unaffected by incorporation into basalt.

Basu assumed a newtonian rheology for alkali basalt magma when calculating nodule settling rates. This assumption is invalid as magmas commonly possess a yield strength at subliquidus temperatures. Sparks *et al.*³ have considered the effect of non-newtonian rheology on the transport of xenoliths by magmas. They conclude that blocks of the sizes observed have zero settling velocity in the majority of magmas. Thus, Basu's calculation of magma ascent rate cannot be justified.

In xenolith suites where a range of rock types is represented, fragment angularity is highly variable and unrelated to mineralogy or depth of origin.

Non-newtonian magma rheology favours xenolith transport by slow, rather than rapid, ascent of magma³. Thus xenoliths are likely to have been in a state of internal chemical and mechanical disequilibrium for a considerable time before their arrival at the surface. Brittle failure occurs as a response to changing conditions after incorporation of a xenolith into rising magma. Angular ultrabasic blocks from La Palma, Canary Islands, show such clear evidence of disequilibrium as partial melting induced by heating by the host magma (my unpublished data). Ultrabasic xenoliths in basalts should be regarded as unreliable guides to dynamic conditions in the mantle.

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BASU REPLIES—Central to Wolff's criticism is the conclusion by Sparks *et al.*¹ that the abundance of ultramafic xenoliths in alkalic basalts is due to the slow rates of ascent of such magmas from mantle depths. Using thermal diffusivity arguments based on such measurements in olivines, Wolff also suggests that blocks of ultramafic xenoliths will attain thermal equilibrium with their enclosing basalts in a matter of hours.

The xenoliths under discussion and other associated xenoliths in the same lava flow in San Quintin volcanic field show evidence of strong plastic deformation. My conclusion that these xenoliths could not have spent longer than a few hours in the ascending magmas is also compatible with conclusions based on recovery kinetics in deformed olivines^{2,3}. The deformed porphyroclasts of olivine in these xenoliths are expected to be completely recrystallized in a few hours due to the relatively fast kinetics of grain growth in conditions of high temperature thermal equilibration with the host lava. The survival of the plastically deformed porphyroclasts of olivine attests to their very short-lived association with the host basalt. Thus, Wolff's contention that "brittle failure occurs as a response to (slowly) changing conditions after incorporation of a xenolith into rising magma" is untenable.

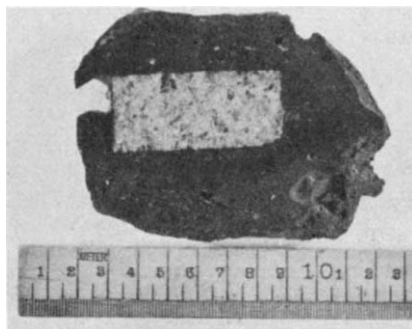


Fig. 1 Perfectly rectangular block of ultramafic xenolith in alkalic lava from the Mt Schank volcano in SE Victoria, Australia. (Photograph courtesy of Dr Alan Moore, University of Cape Town, South Africa.)

Wolff favours a non-newtonian basalt rheology for slow xenolith transport and suggests that the "xenoliths are likely to have been in a state of internal chemical and mechanical disequilibrium for a considerable time before their arrival at the surface." Figure 1 shows an almost perfect rectangular slab of an ultramafic xenolith surrounded on all sides by the alkalic vesicular lava from the Mt Schank volcano in SE Victoria, Australia. Could the orthogonal joint planes in Fig. 1 have

formed by brittle failure as a response to changing conditions after incorporation of this xenolith by the host magma? Or did these joint planes form before the xenolith was included in the magma? The xenolith in Fig. 1 shows typical porphyroclastic texture and evidence of plastic deformation. This evidence alone, because of the nature of the recovery kinetics as discussed above, refutes Wolff's central thesis that the joint planes formed after incorporation of the xenolith by the magma.

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Late Eocene rings around the Earth?

THE suggestion by O'Keefe¹ that the "terminal Eocene event" was caused by rings of tektite material encircling the Earth deserves criticism. O'Keefe assumes tektites to be of cosmic origin and cites his book² in which it is suggested that tektites originate from lunar volcanoes. This assumption is unwarranted and contrary to the numerous existing data^{3–6}. Four specific difficulties are obvious. First, there are no known lunar rocks that are chemically suitable parent materials for tektites or which even appear possibly related to objects of this composition^{3–7}. Second, there are no known lunar rocks of the correct age to satisfy O'Keefe's hypothesis. This is not trivial, as the most recent lunar rocks that have been dated are two orders of magnitude older than those required by O'Keefe. Third, we do not find that the North American tektites fell or were initially deposited throughout a sedimentary rock column of a few million years. Fourth, we have not found even a single tektite with a measurable cosmic ray exposure age, and the detection limits are well below the lifetime of the rings as deduced by O'Keefe.

What then caused the "terminal Eocene event"? I do not propose to answer that question. However, I do suggest that those who are interested in this problem consider the great volume of volcanic ash, air-fall tuff and bentonite (altered volcanic ash and tuff) that occurs in the late Eocene

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sedimentary rocks of the Gulf Coastal Plain from Texas to Georgia⁸⁻¹⁰. Some of these tuffs and tuffaceous sedimentary rocks are similar in composition to the North American tektites⁸ and are the probable target rocks from which the North American tektites were derived by a terrestrial impact. Thus, the terrestrial impact mechanism proposed by Urey¹¹ and others for faunal extinctions and major breaks in the geological record also should be considered, particularly in view of the recent work by Alvarez *et al.*¹² which supports this possibility.

If there ever were rings around the Earth, it is certain that the North American tektites (or any of the other presently known tektites) were never a cosmically derived fraction of those rings.

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O'KEEFE REPLIES—The present issue is whether tektites are cosmic or terrestrial in origin. The main point^{1,2} is that the terrestrial hypothesis is found to conflict with the laws of physics, and these arguments have not been answered. Two examples are given below.

First, tektites are good glasses; that is, even in decimetre-sized pieces they are homogeneous and non-porous, unlike impact glasses. The production by meteorite impact (and immediate distribution over distances of thousands of kilometres) of good glass having very low water content, starting from ordinary rocks or soil, is not possible. The diffusion coefficients are too small to permit rapid homogenization³, and the bubbles will not escape in free flight because they have no buoyancy.

Second, many tektites were obviously shaped by surface tension. Certain hollow tektites, when liquid, were so delicate that a breath (literally) would have destroyed them¹. But the terrestrial origin idea demands non-isotropic launch pressures of over half a million atmospheres (50 GPa), followed by entrainment in air behind a shock wave capable, as a minimum, of blowing out the top of the atmosphere⁴.

As regards King's first difficulty, lunar quartz monzonites and rhyodacites having tektitic major-element composition have been reported⁵⁻⁷.

On his second difficulty, note that terrestrial obsidians are also largely confined to the Cenozoic⁸, and further that although most lunar basalts are more than 3,000 Myr in age, others⁹ are distributed over younger ages.

The remaining two difficulties and the conclusion are invalidated by the fact, which I had mentioned, that the (dominant) solar Poynting-Robertson effect seems to move the particles outward.

I have discussed elsewhere^{2,10} the detailed chemical arguments in King's references, and my discussion of them has not been answered. Those arguments are, in any case, merely appeals to plausibility, which should not persuade us to accept violations of physical law.

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Proposed fossil tree shrew genus *Palaeotupaia*

CHOPRA and Vasishat¹ described a skull fragment with partial dentition of a fossil tree shrew (family Tupaiidae) from Miocene Siwalik deposits in India. Together with a maxillary fragment and an isolated lower molar from the same locality², and some incomplete craniodental remains from the Miocene Siwaliks of Pakistan³, these specimens provide the first documentation of the fossil history of tree shrews. No generic or specific allocation was attempted for the Pakistani fossils or for the maxillary and isolated dental remains from India.

In contrast, Chopra and Vasishat¹ assigned their skull fragment to the new genus and species *Palaeotupaia sivalicus*. Although acknowledging that *Palaeotupaia* closely resembles *Tupaia*, they asserted that generic distinction was warranted because of "morphological differences and the large age gap between

our specimens and the living genus". However, their only discussion of differences between the two genera was limited to enumerating several cranial and dental traits that distinguish between *Palaeotupaia* and *Tupaia minor*. All the supposed differences of *Palaeotupaia* (proportionately longer face, less posterior incisive foramina, distinct protocone on P³, more transverse P⁴, and divided mesostyles on upper molars) occur in some species of *Tupaia*⁴⁻⁶. No assessment was presented of the possible primitive or derived nature of resemblances among Siwalik fossils and extant tupaiids. Few, if any, dental traits of *Tupaia* are uniquely derived within the subfamily Tupaiinae. Although at least two derived cranial features (posterior palatal vacuities and enlarged zygomatic foramen) distinguish *Tupaia* and *Lyomys* from other tupaiines^{6,7}, these regions are unfortunately missing from both the Indian and Pakistani fossil skull fragments. Finally, the geological age of the Indian skull fragment is not a biological attribute and is irrelevant in evaluating its possible generic affinities. There are several extant eutherian genera whose geological history extends back to the Miocene or earlier, including the chiropteran genera *Rhinolophus*, *Hipposideros*, *Megaderma*, and *Myotis*⁸.

Because no essential differences in craniodental morphology which might serve to distinguish between *Tupaia* and *Palaeotupaia* were identified, it is premature to propose generic distinction for the Indian Siwalik skull fragment. Instead, the evolutionary relationship of this fossil can be expressed best by either including it questionably in the genus *Tupaia*, or, perhaps more appropriately, by stressing its essentially modern aspect while withholding generic allocation until more complete specimens are recovered, or the holotype of *Palaeotupaia* is studied more thoroughly.

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